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Editorial

The Pathogenesis of Arteriosclerosis

NO DISCUSSION is valid without a definition. The time is long past when any hardening of an artery was labeled "arteriosclerosis." This is now particularly pertinent because arteriosclerosis and atherosclerosis are more sharply defined. I[1] have tried to show that morphologically one can exist without the other and that atherosclerosis when it does occur is but a facultative lesion of arteriosclerosis. There is no arbitrary need to define arteriosclerosis. Biologically speaking it defines itself; since if one studies the maturation of arteries from birth to the senescent years two morphological changes become manifest, first a collagenous thickening of the intima and later a reduplication of the elastica. These are universal lesions and are present in all animals who have a vascular system such as our own and who live long enough. Other things being equal these lesions increase in intensity and extent with age. This applies as well to the lower animals.[2,3]

ARTERIAL CHANGES WITH AGE

Being omnipresent, these two lesions may not be viewed as abnormal but as part of the normal involuntary changes that arteries undergo from birth to old age. In contrast to other organs the arteries do not attain their maximum histologic differentiation at birth but continue to grow as the years progress. At birth there is hardly any intima. The endothelium lies directly upon the elastica which is only a single layer. A distinct collagenous layer of intima already becomes visible at the end of the first year. The following data taken from Schafer's Histology[4] shows the measurements of the intima at different ages:

Age	*Intima* (μ)
Birth	6
10 yr	54
35 yr	124
50 yr	181
70 yr	190

Reduplication of the internal elastica also begins as early as the second year in the larger arteries and involves the small vessels after middle life.[5] The progressive thickening of the intima and of the elastica differ in intensity whether the artery is of the elastic or muscular type but they are never absent in the course of growth. The term "hyperplastic" arteriosclerosis has been applied to this normal involutionary morphogenesis. If, therefore, hyperplasia of the intima and of the elastica may be viewed as the inescapable earliest lesions, then arteriosclerosis is not always an aging phenomenon as currently viewed but begins at birth. Fortunately clinical and anatomic arteriosclerosis are not always coexistent.

This biologic interpretation of arteriosclerosis explains the difficulty some observers have had in determining when physiologic aging ends and disease begins. For instance, Brenner[6] reports an incidence of 80 per cent arteriosclerosis of the pulmonary artery, his criterion

being the thickening of the intima. In his observations the only normal pulmonary arteries occur in children. Anatomically, Brenner is perfectly correct, but when the incidence is calculated according to the gross or naked eye appearance of arteriosclerosis in the pulmonary artery which is determined by lipoid deposits in the intima, the incidence is only six per cent. This latter observation as we shall see has a deep significance in respect to pathogenesis.

Arterial Changes and Pressures

The progressive hyperplasia of the intima and of the elastica may be justly viewed as compensatory phenomena and in previous studies[7,8] many evidences have been cited that showed that these lesions are compensatory to the prolonged normal arterial pressure. These are:

(1) The independence in incidence between gross arteriosclerosis of the greater or lesser circulations. This is due to the circumstance that the normal pressure in the pulmonary artery is only one-sixth that in the aorta. Gross arteriosclerosis of the pulmonary artery is certainly very rare, unless a hypertension of the pulmonary circulation can be predicated. In a study of hundreds of pulmonary arteries lipoid deposits could not be demonstrated by Sudan stains except when they were already grossly visible.

(2) When hypertension, a hyperkinesis of a normal function, is superimposed, the age limit for the production of arteriosclerosis is lowered and the lesions are intensified. It has been shown that, morphologically speaking, the arterial lesions in hypertensive disease differ in no way from those in normotensive individuals except in degree. Because of the frequency of mitral disease and congenital cardiac disorders, arteriosclerosis of the pulmonary artery is common in the juvenile and even in the infantile years.

(3) Arteriosclerosis is appreciably less in hypotensive individuals.[10] It is notoriously less in patients with active tuberculosis, age for age.

(4) The effect of intravascular arterial pressure is well exemplified in the intensification of the lesions at points where the pressure is exerted against an external resistance, for instance, on the posterior wall of the thoracic and abdominal aorta; at the site of vascular fixation, such as at the origin of the intercostal vessels; in the portions of the wall of vessels of the dura that lie next to the bone; in those sections of the pulmonary artery that lie against the rigid bronchus; and in the endocardium directly opposite a perforation of the ventricular septum. Carrel's[11] observation is especially pertinent. He showed that a vein interposed between the divided ends of an artery showed in time a markedly thickened intima. The effect of pressure is negatively exemplified in phlebosclerosis. Since the pressure in the veins is close to zero, thickening of the intima, even in senility, never occurs except in instances where a prolonged venous pressure can be demonstrated, for instance, in the vena cava, hepatic and pulmonary veins in prolonged congestive failure; in the portal vein in hypertension of the portal circulation; in the saphenous veins in varicosities; and in the venous segment of an arteriovenous aneuryism. In passing I may say that hyperplasia of the elastica rarely occurs in veins even when the intima is profoundly thickened. These lesions in the veins are particularly impressive for our thesis because even with the most aggravated and prolonged venous pressure, for instance, in constrictive pericardium, it never even approaches the normal systemic arterial pressure.

The testimony adduced affords decisive evidence in my opinion, that the prolongation of the normal intraarterial pressure is the main conditioning factor in the production of the earliest lesions of arteriosclerosis. In other words, we maintain that a normal function sufficiently continued can ultimately cause vascular disease sufficient at times to compromise life. I have suggested therefore the following equation:

$$\text{arteriosclerosis} = \text{intravascular pressure} \times \text{time}$$

Apparently, Thoma's[12] third law of the growth of vessels, namely, that the thickness of a vessel is dependent on the difference between intravascular and extravascular pressure, which he applied to the embryonal development of arteries, is perfectly applicable to postembryonal growth. The important conclusion from the

premises we have submitted is that arteriosclerosis of the greater circulation as manifested by hyperplasia of the intima and elastica is not reversible because normal intravascular pressure cannot be abolished without compromising life itself.

Teleologically, the hyperplasia may be viewed as an adaptation to the progressive rise of intraarterial pressure that normally proceeds from birth to old age, or if there is no perceptible increase, to the prolonged maintenance of the normal pressure. In other words, a pavement will be worn out by vehicles, but the process will take longer with lighter vehicles than heavier ones.

Arterial Degeneration

The hyperplasia of the intima and elastica may be the only lasting lesions of arteriosclerosis; this applies especially in the pulmonary circulation. However, in the further evolution of arteriosclerosis other lesions become superimposed, generally classified as degenerations. I refer to fibrosis and the deposition of a metachromatic substance consisting of mucopolysaccharides in the walls of the vessel. This deposit is already visible in children[14] and increases with age.[15–17] In addition, there may be hyaline, mucoid, calcareous, and lipoid degeneration. Of these later changes, the only one worth serious consideration is the lipoid deposition, in other words, atherosclerosis, a phase of vascular disease that in recent years has stimulated a vast amount of study. The importance of atherosclerosis looms large not only because it is the deposition of lipid in the intima that renders arteriosclerosis visible grossly, but also because it largely contributes to the narrowing of the lumen. Furthermore, atherosclerosis lends itself to experimental reproduction and its elimination or prevention has aroused hopes that its ravages, especially in respect to the rising incidence of coronary disease, may be controlled.

Experimental Atherosclerosis

The experimental study of atherosclerosis was begun by Anitschkow and Chalatow[18] nearly forty years ago by cholesterol feeding to rabbits. There is no doubt that the deposits of lipid mimicked those occurring in human beings, but there were impressive differences, the most striking being the lack of selective distribution to the arterial tree and the fact that it was produced by unphysiologic means and then only in herbivora. Since then some of these differences have been overcome,[19,20] but two noteworthy differences remain: first, the circumstance that in experimental atherosclerosis there was no linear relationship to the blood level of the cholesterol (this is largely dependent on species difference); and second, that human atherosclerosis is unaccompanied by a hypercholesterolemia except in the nephrotic syndrome, hypothyroidism, prolonged biliary obstruction, and in essential or familial hypercholesterolemia. A number of attempts have been made to explain these discrepancies by chemical or physical differences in the composition of the plasma lipids; for instance, it has been shown that the development of atherosclerosis sometimes depends upon the ratio of the cholesterol to the plasma phospholipid. Barr and his co-workers[21] have in addition studied the distribution of the alpha and beta lipoproteins in the plasma in different animals, in infants, young men and women and in human conditions associated with atherosclerosis. Gofman's studies[22] of the lipids with the ultracentrifuge are familiar. Both Barr's and Gofman's studies, while suggestive, have the same defect, namely, that their findings bear only an approximate but not a consistent relation to the incidence of atherosclerosis.

Thus far no method has been devised of measuring the lipids in the blood quantitatively or qualitatively by physical or chemical methods which afford any ability to predict the incidence of atherosclerosis. The problem is rendered difficult because such studies take into consideration only one factor, important as it may be, that enters into the production of atherosclerosis, namely the lipid content of the blood. Most observers fail to consider that the blood always contains a certain quota of cholesterol and other lipids. It is not a question of either/or but only of more or less. In other words, in respect to the blood cholesterol the most we can hope for is a partial but not a complete solution of the problem.

Factors in Atherosclerosis

Other factors enter into the production of atherosclerosis, viz.:

(1) *Hypertension:* The fact that atherosclerosis is more pronounced in hypertensive states is acknowledged, and accounts largely for the atherosclerosis observed in the juvenile years. Gross atherosclerosis of the pulmonary artery is practically always associated with prolonged hypertension of the pulmonary circulation. Faber[23] showed that experimental atherosclerosis can be produced even with a normal blood cholesterol provided hypertension is induced. A highly confirmatory evidence of the effect of hypertension upon atherosclerosis is a negative one, namely, that atherosclerosis is exceedingly rare in phlebosclerosis.[24] In examining hundreds of portal, hepatic, pulmonary veins, and the vena cava, I have seen atheroma in phlebosclerosis, but very rarely.

(2) *The Changes in the Vessel Wall Previously Described:* There is abundant testimony that injury of the vessel wall predisposes to the deposition of lipid in the vessel wall; this includes injury produced by adrenalin,[18] detergents,[25] cauterization,[26,27] scurvy,[28] and syphilis. Many observers believe that the mucopolysaccharides act as precursors to the deposition of lipid.

In sectioning many arteries I have never found lipoid deposition in the intima unaccompanied by a hyperplasia of the intima. Wilens[29] contends that the intimal thickenings are secondary and the results of the lipid deposition; but the fact that reverse relationships exist in the pulmonary artery is a valid argument that the same sequence occurs in all arteries. Moon and Rinehart[30] demonstrated in coronary atherosclerosis that thickening of the intima preceded the deposition of lipid. Also, they showed that the fibrous plaques that followed the induction of experimental atherosclerosis bore little resemblance to the histogenesis of human coronary atherosclerosis.

(3) Finally, the *Dynamic Factor of Time:* The neglect of this factor explains why all attempts to formulate linear relationships between experimental factors and atherosclerosis have thus far failed. Anitschkow recognized the time element years ago when he showed that atherosclerosis can be produced with a lesser degree of hypercholesterolemia if the experiment is prolonged. In other words, it will take longer to produce atherosclerosis with a normal cholesterolemia and a normal blood pressure than with a hypercholesterolemia and it will take a lesser time to cause an atherosclerosis with a hypertension or a hypercholesterolemia. The time factor probably explains some of the species difference in the incidence of arteriosclerosis since by and large, the longest lived animals, at least in terms of their captivity, show the highest incidence of arteriosclerosis.[2,3] The greatest incidence is in birds who are notoriously long lived. Certainly in every field except experimental atherosclerosis, in pulmonary hypertension and in juvenile hypertension of the greater circulation, atherosclerosis is a senescent phenomenon. Statistical studies on the incidence of atherosclerosis in different sections of the vascular tree are valueless unless the time factor is considered.

The evidence is strong that most of the lipid in atherosclerosis arises by direct imbibition from the plasma, for the following reasons: First, there is a striking similarity in chemistry and in the distribution of the lipid in the plasma and in the arterial wall. Second, in experimental and human atherosclerosis the initial deposit is in the intima. Third, there is an increase in the amount of lipid in hypertensive states, whether of the greater or of the lesser circulations. Conversely, in hypotensive states the amount is less. Fourth, Anitschkow showed that the lipid was deposited in the same areas that revealed the greatest permeability to colloidal dyes such as trypan blue. Fifth, in hypercholesterolemia the deposits are greater than in normocholesterolemia. Most convincing is the work of Wilens[31] who showed experimentally that with sufficient pressure, lipid could be expressed into the wall of vessels. Inasmuch as the plasma lipid exists in a colloidal form and in the artery as a granular deposit, the presumption is that the intima takes part in this transformation. Not all the lipid enters the vessel wall by imbibition. Winternitz and his co-workers have adduced convincing evidence that some lipid is the result of hemorrhage from the rupture of the intimal capillaries.

There is no doubt that experimental atherosclerosis is reversible, that is, the lipid disappears if the experiment is stopped at a proper time, even though connective tissue changes persist in the wall of the artery. But there is strong doubt whether human atherosclerosis is reversible, even partially, because the most important elements that enter into its production, namely normocholesterolemia, intravascular pressure, the changes in the ground substance and the time factor cannot be eliminated. The most that can be hoped for is a cessation or a slowing of the process. The only conditions in which human atherosclerosis may be reversible is in the hypercholesterolemic states previously mentioned.

It is obvious that owing to the numerous interacting factors that enter into the production of arteriosclerosis, a complete reversal or a prevention will be an unattainable project. That is why arteriosclerosis has always been with us, in antiquity,[32] and all climes, in all races. It is an inescapable destiny.

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Symposium on Coronary Disease

Clinical Aspects of Coronary Heart Disease*

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During the past twenty years few diseases have received more attention than coronary heart disease. This attention is warranted since it has for some years been the most common form of heart disease in people over the age of forty, and with the aging of our population the incidence is increasing. Recent reports[1–3] suggest that the frequency of this disease in young persons is also increasing. Meanwhile, recent major advances in the prevention and treatment of other types of heart disease, such as rheumatic, luetic, infectious and congenital, have so reduced the mortality from these causes that coronary heart disease is causing an even greater proportion of all cardiovascular deaths.

Although Heberden in 1768[4] first introduced the term angina pectoris and some years later Jenner[5] related this syndrome to heart disease, it was only after Herrick's classic description of coronary occlusion in 1912[6] that clinical investigations began to appear.

During the past 30 years the number of reports concerning coronary heart disease has increased almost geometrically. The continuing flood of papers provides convincing evidence, however, that we are still far from solving the problems of this serious disease.

The designation "coronary heart disease" has come more and more into common use and is justifiably supplanting the older term "arteriosclerotic heart disease." Perhaps a slightly more direct and descriptive term from the standpoint of pathologic physiology is that long used by the British, "ischemic heart disease," since the one common denominator of coronary heart disease appears to be myocardial ischemia. For the sake of consistency, the term "coronary heart disease" will be used in this discussion. This term permits inclusion of the very uncommon non-atherosclerotic disease processes which may result in myocardial ischemia.[7] These include: (1) valvular lesions which may alter either pressure or flow in the coronary circulation; (2) luetic ostial stenosis; (3) coronary embolism; (4) hypertension; (5) periarteritis nodosa; (6) anemia; and (7) some congenital diseases of the coronary arteries. However, it seems appropriate for this discussion to consider coronary heart disease as practically synonymous with coronary atherosclerotic heart disease.

Etiologic Factors

The overall incidence of coronary heart disease in males is approximately four times that seen in females.[8] In males the incidence remains low up to the age of 40 and then rises steeply to the age of 60, after which it falls as steeply. Females, on the other hand, show a slow but steady increase in incidence from 40 to 70 years of age. Thus, between the ages of 50 and 59, the male to female ratio is ten to one, while after the age of seventy, it is less than two to one. In a recent study comparing myocardial infarctions in the white and Negro races,[9] an unexpectedly high incidence of myocardial infarction was found in Negro females so that the male to female ratio was approximately one to one. In this same study, the incidence of coronary heart disease in Negroes was approximately one-half the incidence in Caucasians.

The increased incidence of coronary heart

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disease in patients with both diabetes and hypertension is well established.[10] Genetic factors have also been studied[11] but the statistical data thus far do not delineate the relationships. There does appear to be a high incidence of coronary heart disease in the so-called "mesomorphic" or "masculine" body type.[12] These findings are in accord with the greater incidence of coronary heart disease in males and fit well into current concepts of the relationship between gonadal hormones and atherosclerosis.

Extensive studies during the past few years have shown that the sera of normal young women have a relatively smaller concentration of beta lipoprotein and a higher concentration of alpha lipoprotein than the sera of normal young men,[13] but this difference between the sexes is not apparent after the menopause. Ultracentrifuge studies[14] have also shown lower concentration in women of the so-called "atherogenic" lipoproteins of the Sf 10–100 classes. Further work in this area includes reports of the effectiveness of estrogens in reversing experimental coronary atherosclerosis in the cockerel[15] and the fall in serum beta lipoprotein and cholesterol levels following estrogen administration to survivors of myocardial infarction.[13] At the present time, several long-term studies are attempting to evaluate the therapeutic aspects of estrogen in coronary heart disease.

The other current area of large-scale investigation is the role of diet, particularly the content of fat in the diet. Extensive studies by Keys' group have demonstrated a good correlation between the per cent of fat in the diet, the serum cholesterol, and the incidence of coronary heart disease.[16] They have also reported that reduction of dietary fat is accompanied by reduction in serum cholesterol levels.

Manifestation of Myocardial Ischemia

Although the nature of the atherosclerotic process is still unsolved, our understanding of the pathogenesis of the resulting myocardial disease appears to be on firmer ground. There is substantial agreement that clinical coronary heart disease is an expression of varying degrees of myocardial ischemia and anoxia.[17–20]

The two general mechanisms through which myocardial ischemia and anoxia may occur are: (1) Those factors which reduce the supply of blood or oxygen to the myocardium. These include coronary artery narrowing or occlusion; decreased coronary artery pressure, as in shock and hemorrhage; decreased coronary artery flow as in arrhythmias, congestive failure, or aortic stenosis; inadequate oxygen transport as in anemia, pulmonary insufficiency, high altitude or carbon monoxide poisoning; (2) Those factors which increase the heart's demand for oxygen. These include exercise, digestion of food, fever, infections, emotion and hyperthyroidism.

The occurrence and degree of myocardial ischemia will depend upon the adequacy of the myocardial blood and oxygen supply in meeting the work requirements of the heart. A transient period of relatively mild and reversible myocardial ischemia is the physiologic disturbance which clinically produces angina pectoris. With somewhat more intense ischemia, or involvement of a wider area, or some prolongation of the ischemic state, the anginal symptoms will be more severe.

Angina Pectoris: The primary symptom of angina pectoris is pain of a constricting character, usually substernal or precordial radiating to the throat or arms, usually brought on by exertion, intense emotion, ingestion of food, or exposure to cold. Relief of pain may in some cases be obtained simply by rest. Relief of pain by nitrites is so striking and so frequent that this response is considered important in the diagnosis of the anginal syndrome.

Less frequently, anginal pain may be atypical in location, may occur at rest or only on initial effort. There are usually no gastrointestinal manifestations, no fever, leukocytosis or increase in sedimentation rate. After the pain has subsided, the patient feels and appears to be normal. The blood pressure does not fall and the electrocardiogram may be normal or may show transient RS-T and T wave changes during or shortly after the pain. Frequently, the typical anginal attack may be produced by either exercise or by induced anoxemia. Because of this fact, both exercise and anoxemia tests are sometimes useful aids in diagnosis of the obscure case.[21–24]

Myocardial Infarction: At the other end of the spectrum of coronary heart disease is the picture of severe myocardial infarction. Here the myocardial ischemia is intense, extensive, prolonged and irreversible. Severe precordial, retrosternal, or upper abdominal pain of a crushing or constricting character is usually present and frequently radiates to the throat and arms. It may persist for many hours or even several days. In some cases of myocardial infarction the patient may deny pain, but almost always there is some discomfort which can be elicited by careful questioning. Nausea and vomiting commonly occur and are thought to be reflex in origin. Shock of varying degree often is present and arrhythmias are common. Pericardial friction rubs are present more commonly in anterior than in posterior myocardial infarction but often are so evanescent that they will be missed unless auscultation is repeated several times a day. Left ventricular failure with dyspnea and acute pulmonary edema may ensue. Leukocytosis usually will occur within 12 hours and fever within 24 hours. Serum glutamic oxalacetic transaminase usually rises within 12 hours and falls to normal within 72 hours. The sedimentation rate, which may be normal initially, usually begins to rise in two to three days. The electrocardiogram commonly exhibits characteristic RS-T segment, T wave and QRS abnormalities within a few hours after the infarction, with serial changes thereafter.

Between mild angina pectoris on the one hand, and severe myocardial infarction on the other are various gradations of myocardial ischemia, which depend on the intensity and duration of myocardial anoxia and the size and location of the area involved. Such gradations would include the stages from mild to severe angina pectoris, and at the other end from severe to mild myocardial infarction.

Intermediate Syndromes: Somewhere in the midst of these gradations, an intermediate syndrome has been proposed as a clinicopathologic entity termed most commonly "acute coronary insufficiency,"[25–27] but also called "coronary failure,"[28] and the "intermediate coronary syndrome."[29] These terms are applied to groups of symptoms in which cardiac pain is more severe or prolonged than in simple anginal attacks, but in which there are neither typical signs nor the characteristic electrocardiographic patterns of myocardial infarction. The electrocardiogram in these cases usually shows RS-T depressions with or without T wave inversions.

There have been frequent objections to the expression "acute coronary insufficiency" because the term itself is quite confusing and because of doubt as to whether it represents a true clinical entity. The name itself is confusing since "coronary insufficiency" has a general physiologic meaning akin to terms such as "pulmonary insufficiency," "renal insufficiency" and "hepatic insufficiency" in which a general failure of function is implied. In like manner, the term "coronary insufficiency" has long been used in this general sense.[22] This terminology certainly would be expected to confuse medical students already beset with a new and complex scientific vocabulary.

The second objection to the syndrome of "acute coronary insufficiency" comes from those who believe that it is not a distinct clinical entity, but merely includes cases of severe angina pectoris on the one hand and mild myocardial infarction on the other. The concept of this intermediate syndrome has been welcomed by many practicing physicians because of the frequent problem presented by the patient with persistent anginal pain unrelieved by nitroglycerin, and with only RS-T and T wave changes in the electrocardiogram. In one type of case, the temperature, white blood count and sedimentation rate may be normal. Since the doctor is faced with the possibility that this picture may usher in an episode of typical myocardial infarction, the patient is frequently hospitalized. When there is rapid regression of the signs and symptoms, together with the return of the electrocardiogram to normal, the patient may be discharged from the hospital with the diagnosis of "acute coronary insufficiency" since the doctor desires to indicate that this episode was more severe than the usual attack of angina pectoris. There is implicit in this reasoning an assumption that angina pectoris itself is relatively benign. Physicians often consider attacks of angina pectoris to be

completely reversible. That this concept is open to question is illustrated by the necropsy findings of focal necrosis and diffuse myocardial fibrosis in patients with long standing, but typical angina pectoris.[20] The serious nature of the process has been reemphasized by a recent investigation of its natural history.[30] In this study, 40 per cent of 158 patients with typical angina pectoris developed minor to major myocardial necrosis, 23 per cent developed classic myocardial infarction, and 16 per cent experienced sudden unexpected death. It would seem much more logical, therefore, to designate these intermediate clinical pictures as "severe angina pectoris with protracted myocardial ischemia." In this way, the close relationship between the typical angina of effort and the protracted angina at rest may be emphasized.

The diagnosis of "acute coronary insufficiency" is also applied to the patient with the same protracted anginal pain and RS-T and T wave changes without characteristic Q changes who also exhibits fever, leukocytosis, some elevation of the sedimentation rate, and a more protracted course. Here, different problems face the physician. He may be inclined to consider this process "mild myocardial infarction" since the histopathologic findings usually show varying degrees of subendocardial infarction, but the words "myocardial infarction" carry unpleasant connotations. He must face the problem of "bed rest or not, and, if so, how long?" and whether or not to institute anticoagulant therapy. For some physicians, the diagnosis "acute coronary insufficiency" provides a protective haven from these difficult decisions, particularly since many have been conditioned to the rather rigid regimens previously advocated for all patients with acute myocardial infarction. The solution of this problem lies rather in review and revision of the therapeutic concepts, with emphasis on the fact that myocardial infarctions of varying severity may well have different therapeutic needs. It has long been realized that the therapy for a bleeding peptic ulcer with only transient melena differs greatly from the treatment of the patient with a bleeding ulcer producing massive hematemesis and shock. Yet, it has not been necessary to split these into separate diagnostic categories.

The following case illustrates the folly of attaching a clinical label such as "acute coronary insufficiency" to a phase of a progressive picture which may slowly, rapidly or erratically progress from one end of the spectrum to the other. The clinical and laboratory findings depend as much upon the speed of progression and the duration of the process as upon the magnitude of the myocardial involvement.

Case History

A 55-year-old obese brewery worker was first seen on November 18, 1954 because of recurrence of chronic duodenal ulcer. Hypertension was known to have been present for thirty years.

Physical examination revealed Grade II K-W retinal changes, a blood pressure of 174/110 and a heart without abnormal physical signs. Complete blood count, urinalysis, sedimentation rate and serology were normal. Serum cholesterol was 280 mg/100 ml. Chest x-ray was normal. Electrocardiogram (Fig. 1A) revealed low T in lead I and an inverted T wave in aVL.

Medical ulcer management was followed by long lasting relief of all symptoms. Reserpine, 0.5 mg daily, effected a reduction in blood pressure to the range of $\frac{134\text{–}150}{80\text{–}86}$.

In September 1956, the patient first complained of aching of the throat, extending to the shoulders, occurring with mild exertion or severe emotion, but not after eating. This distress was immediately relieved by rest. He did not consult a physician until November 1956, when an electrocardiogram (Fig. 1B) revealed inversion of the T waves in V_{4-6}. Nitroglycerin was employed and gave immediate relief from pain.

He continued work until December 11, 1956, when he wakened from sleep at 1:30 a.m. with a recurrence of the above described pain associated with sweating, vomiting and dyspnea. No relief was obtained from three nitroglycerin tablets. The patient was hospitalized immediately and was given morphine sulphate, 32 mg, and nasal oxygen with incomplete relief of pain. Acute left heart failure rapidly ensued, requiring intravenous digitalization with lanatoside-C. Electrocardiogram revealed more extensive T inversions than previously noted, but no significant Q deflections. Complete blood count, sedimentation rate and serum glutamic oxalacetic transaminase were normal. Electrocardiograms repeated December 12, 13, and 14, 1956 (Fig. 1C) showed no changes, despite temperature elevations from 100° to 101° F on December 13 and 14, 1956, and daily recurrences of the pain requiring opiates every 8 or 12 hours. On December 18, 1956 he again had a temperature elevation to 102° F which persisted 48 hours, then falling to normal levels where it remained throughout his hospitalization.

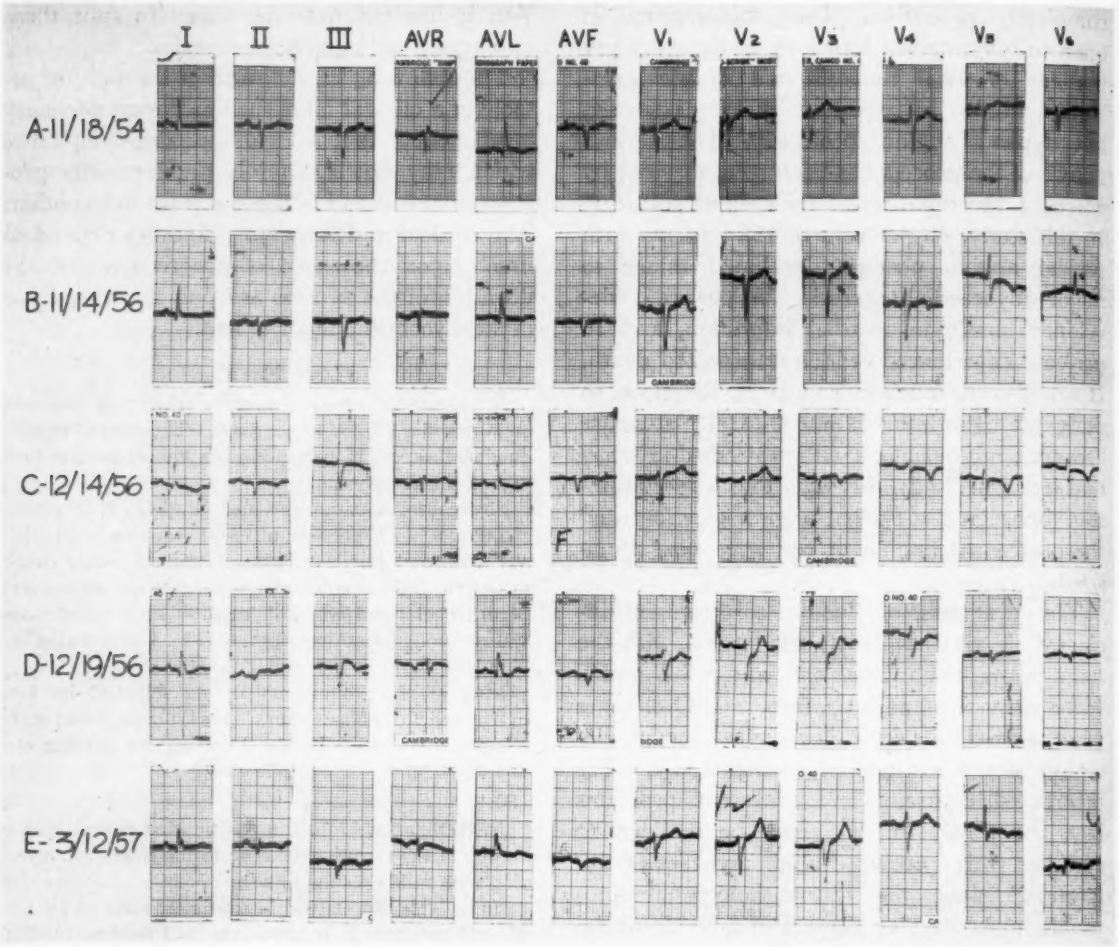

Fig. 1. Serial electrocardiograms on patient whose clinical course is outlined in the Case History. See text.

On December 19, 1956 a friction rub became audible at the base of the heart and a repeat electrocardiogram (Fig. 1D) revealed ST deviations and significant Q deflections suggesting a postero-lateral myocardial infarction. The E.S.R. rose from 5 to 37 mm per hour and serum glutamic oxalacetic transaminase was thirty-seven units. C-reactive protein showed a trace in two and twenty-four hours. On December 20, 1956 the WBC rose to 10,800 with 6 per cent stab forms and 72 per cent segmented forms. By December 25, 1956 all symptoms had subsided and convalescence was uneventful. He was discharged from the hospital January 7, 1957 ambulant and returned to work March 12, 1957. Since then he has experienced occasional angina requiring nitroglycerin for relief. An electrocardiogram March 12, 1957 (Fig. 1E) revealed the pattern of a stabilized postero-lateral myocardial infarction.

This case provides a "capsule demonstration" of the spectrum of coronary heart disease in which classic angina pectoris was followed by an episode of protracted myocardial anoxia which progressed to the pattern of actual myocardial infarction.

Congestive Heart Failure

Next in importance in coronary heart disease is congestive heart failure, which may occur after an acute myocardial infarction, after a previous history of angina pectoris, or as the initial clinical manifestation. The heart failure immediately following myocardial infarction is thought to result chiefly from the acute anoxia to the left ventricle, that occurring later, to the scarring and loss of muscle. In long standing angina pectoris, diffuse myocardial fibrosis is the probable cause. Where congestive heart failure is the initial clinical man-

ifestation of the heart disease, the same diffuse myocardial necrosis or fibrosis is usually implicated, often initiated by such secondary factors as fever, anemia, tachycardias or unusual exertion.

The initial heart failure is usually left-sided because: (a) the coronary arteries supplying the left ventricle are most damaged by atherosclerosis; (b) infarcts occur primarily in the left ventricle; and (c) the larger left ventricle performs more work and is, therefore, more susceptible to anoxia. The characteristic symptoms are paroxysmal cough and dyspnea, frequently nocturnal, together with weakness and fatigability. Right-sided heart failure with hepatic enlargement, venous engorgement and peripheral edema may occur secondary to the left-sided heart failure, occasionally is primary, and in some cases appears almost simultaneously.

Cardiac Arrhythmias

Among the other important clinical manifestations of coronary heart disease are the cardiac arrhythmias. Most commonly encountered are ectopic rhythms including premature ventricular contractions, atrial fibrillation or flutter and atrial, nodal, or ventricular tachycardias. These ectopic rhythms are relatively common and are thought to result from increased irritability of an ectopic focus so that it emits rhythmic stimuli with greater frequency than the sinus node. Less frequent than ectopic rhythms are the disturbances in conduction of the cardiac impulse. Atrioventricular heart block and bundle branch block are the most common examples. These conduction disturbances usually indicate that a portion of the myocardial conduction system has been damaged by protracted anoxia, infarction or fibrosis. Not uncommonly, however, they are toxic manifestations resulting from treatment of the underlying heart disease.

In bundle branch block, there is a delay in or obstruction to the conduction of impulses in one of the branches of the bundle of His. The diagnosis of these conduction defects can be made with certainty only from the electrocardiogram. Not infrequently, the electrocardiographic finding of bundle branch block in asymptomatic persons is the sole clue to the presence of coronary heart disease, but caution must be exercised lest an electrocardiographic abnormality which is comparatively innocent be used incorrectly to diagnose heart disease.

Sudden Death

One of the common terminations of either angina pectoris or acute coronary occlusion is sudden death. It has been estimated that sudden death occurs in over 27 per cent of patients with a history of cardiac pain and 9 per cent of those without such pain.[31] In an analysis of 950 autopsied cases of coronary artery disease from the Armed Forces Institute of Pathology, sudden death occurred in over 40 per cent of the cases.[32]

Although sudden death in coronary heart disease may result from acute massive pulmonary embolism, rupture of the myocardium, etc., the majority of such deaths are thought to represent so-called "mechanism" deaths, which include ventricular fibrillation and cardiac standstill. A recent experimental study has resulted in the concept that ventricular fibrillation in the laboratory animal could be triggered by the electrical instability resulting from a current of oxygen differential at the boundary between an anoxic area and surrounding normal myocardium.[33] Conversely, uniformly anoxic hearts were found to be electrically stable and arrhythmias uncommon. Perfusion of a limited area of such an anoxic heart with oxygenated blood often produced a "reverse trigger" type of instability with resulting ventricular fibrillation. These interesting observations, in addition to helping explain the onset of ventricular fibrillation, may have therapeutic implications.

Diagnosis of Chest Pain

The diagnosis of angina pectoris may at times prove difficult. Of the twenty or more conditions which may simulate angina, musculoskeletal abnormalities of the lower cervical or upper dorsal spine have been of much interest. The differentiation of this "root pain" from angina pectoris can usually be accomplished without much difficulty. The more difficult problem arises when the two conditions coexist.

We have seen such patients in whom the diagnosis of angina pectoris was established by history and confirmed by exercise and anoxemia tests. Response to nitrites in such patients may be dramatic at times and at other times ineffectual. The discovery of cervical spine abnormality by x-ray and subsequent therapeutic trial of neck traction has demonstrated that two similar types of pain may occur, the anginal pain which responds to nitroglycerin, and the "root pain" which responds to neck traction or other orthopedic measures. In other instances, reflex impulses of musculoskeletal or other origin may initiate anginal attacks. Treatment of the underlying process may then relieve the angina.

A recent contribution to the problem of diagnosis of chest pain is the description of what is termed "The Anterior Chest Wall Syndrome," a symptom complex of unknown etiology consisting of somatic involvement of the anterior chest wall with pain and tenderness, with frequent good response to corticotropin, corticosteroids, or x-ray therapy.[34]

The relation of cardiac pain to coronary occlusion and myocardial infarction is of considerable clinical interest. A recent clinico-pathologic study of coronary heart disease by British workers sheds some light on this subject.[35] In their series of 30 recent myocardial infarcts with coronary occlusion, 76 per cent had pain and 24 per cent were asymptomatic. In contrast, only 43 per cent of 21 recent infarcts without coronary occlusion had pain, the remainder being asymptomatic. It was further noted that the pain was usually severe when infarction resulted from coronary occlusion, milder if occlusion was not present. These investigators emphasized that the *intensity* of the ischemia is the important factor in the production of pain, whereas the *duration* of the ischemia is most important in the production of infarction. It then follows that a degree of ischemia insufficient to cause pain may, if sufficiently prolonged, result in myocardial infarction. There was no correlation between symptoms and either the site or size of the infarction. Finally, the infarcts without pain appeared to do poorly and accounted for a high proportion of the sudden deaths observed.

Summary

Coronary heart disease is the most important problem in the field of cardiovascular disease. The higher incidence of coronary heart disease in males, particularly those of the "mesomorphic" type has been well established. The differences between the male and female serum lipoprotein patterns, and the efficacy of estrogens in reversing the "male" pattern have suggested a definite relationship between the gonadal hormones and atherosclerosis. Convincing evidence has been collected implicating dietary fat in the etiology of coronary heart disease.

The myocardial ischemia and anoxia of coronary heart disease result from two general mechanisms: reduced supply of blood or oxygen to the myocardium and increased myocardial demand for oxygen.

The clinical features of coronary heart disease are presented as a continuous spectrum of varying severity from mild angina pectoris at one end through more severe grades of angina and mild myocardial infarction to severe myocardial infarction at the other end. The clinical and laboratory findings depend as much upon the speed of progression and duration of the process as upon the magnitude of myocardial involvement. The usefulness of the term "acute coronary insufficiency" is questioned both on semantic grounds and because of doubt as to whether this "syndrome" constitutes a true clinical entity.

Recent clinico-pathologic studies of coronary heart disease have emphasized that the *intensity* of the myocardial ischemia is the important factor in the production of pain, whereas the *duration* of the ischemia is of primary importance in the production of infarction.

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Serum Glutamic Oxaloacetic Transaminase, Lactic Dehydrogenase, and Glutamic Pyruvic Transaminase Activity in Evaluation of Heart Muscle Damage*

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GLUTAMIC oxaloacetic transaminase is a specific tissue enzyme affecting the transfer of the α amino nitrogen of aspartic acid to α keto-glutaric acid resulting in the synthesis of a new amino acid, glutamic acid and a new α keto acid, oxaloacetic acid. Acute transmural myocardial infarction is followed by an increase in the activity of this enzyme in the serum.[1] Since the activity of glutamic oxaloacetic transaminase (GO-T) is 5,000 to 10,000 times greater in heart muscle than serum, lactic dehydrogenase (LD) 3,000 and glutamic pyruvic transaminase (GP-T) 1,000 times greater, release of these enzymes from damaged cells probably accounts for the increase in serum activity following acute myocardial infarction (Table I). These enzymes have been found to be present in all human sera tested and can be measured chromatographically, spectrophotometrically, and colorimetrically. Spectrophotometrically a unit of activity is defined as a decrease in optical density of 0.001 mu/ml/min at 23° C.[2] The mean activity in human sera for SGO-T is 22.1 units ± 6.8, for SGP-T 16.0 units ± 9.0 units, and for SLD 400 units ± 200 units.

SGO-T is stable in serum for four days at refrigerator temperatures and loses little activity if stored at these temperatures up to 30 days. The plasma and serum levels are the same, are reproducible from day to day in the same normal individuals, and are unaffected by freezing or lyophilization. Heating to 100° C will destroy the activity.

Myocardial injury results in a decrease of activity of SGO-T in the injured heart muscle and is associated with a proportional increase in the activity of the serum (Fig. 1). The SGO-T is also increased following acute damage of skeletal muscle, liver, and possibly kidney. Central nervous system injury has not been found to be associated with consistent increases in SGO-T activity. The serum transaminase levels rise precipitously after death, and are

TABLE I

The Glutamic Oxaloacetic Transaminase and Lactic Dehydrogenase Activity of Normal Human Organs and Serum

Normal human tissue (u/g of wet tissue)

	GO-T	L-Dase
Heart	155,500	221,600
Liver	142,400	94,700
Skeletal muscle	99,300	160,200
Kidney	90,900	281,800
Spleen	13,600	108,800
Lung	10,000	73,600
Pancreas	28,300	131,200
Serum	20	470

* From the Sloan-Kettering Institute and the Medical Service of the Memorial Center for Cancer and Allied Diseases, New York, New York.

highest in venous reservoirs draining tissues of maximal GO-T activity.

The SGO-T activity does not increase during infectious, degenerative, neoplastic, allergic, reactive or congenital disease states, pregnancy or delivery, *unless* these are associated with acute damage to heart, skeletal muscle, liver, or possibly kidney. There is no consistent relationship between the SGO-T activity and the erythrocyte sedimentation rate, the white blood count or the C-reactive protein levels. The type of hemolysis occurring during routine separation of serum from red blood cells does not significantly alter SGO-T and SGP-T activity but causes a significant increase in SLD.

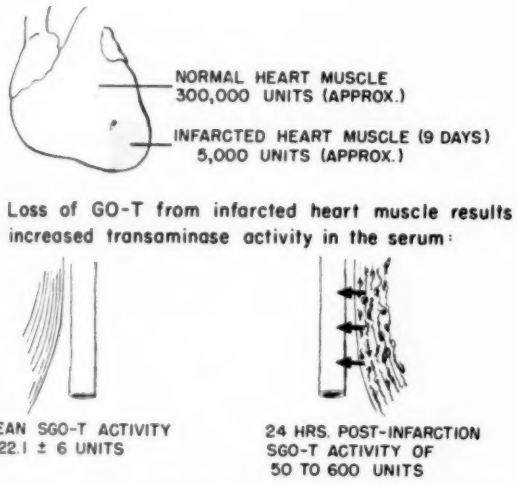
NORMAL HEART MUSCLE
300,000 UNITS (APPROX.)
INFARCTED HEART MUSCLE (9 DAYS)
5,000 UNITS (APPROX.)
Loss of GO-T from infarcted heart muscle results in increased transaminase activity in the serum:
MEAN SGO-T ACTIVITY
22.1 ± 6 UNITS
24 HRS. POST-INFARCTION
SGO-T ACTIVITY OF
50 TO 600 UNITS

Fig. 1. A schematic demonstration of the probable mechanism of increased SGO-T activity following acute myocardial infarction.

Since SGO-T activity has been studied in many more patients with heart disease than SGP-T or SLD, only brief mention of changes in the activity of the latter two enzymes will be made where data are available for comparison.

Experimental and Clinical Findings

Myocardial Infarction

(1) *Experimental:* Myocardial infarction was produced in dogs by the injection of plastic spheres into the coronary sinus. In every experiment the SGO-T activity rose promptly with peak levels appearing 9 to 23 hours post-infarction, sometimes reaching values 20 to 30 times control levels. There was a relatively linear correlation between the amount of infarction estimated at autopsy and the maximal rise in SGO-T activity (peak level). The animals with the highest SGO-T levels had the greatest degree of myocardial infarction.[3] Acute myocardial necrosis resulting from the intravenous injection of papain in rabbits resulted in peak SGO-T levels in individual experiments that were again roughly proportional to the degree of necrosis found at autopsy.

Myocardial infarction was also produced in dogs by tightening a ligature ten days after it had been placed about a coronary artery. Fifteen infarcts produced by this method were all associated with an increase in the SGO-T activity. As in the previous experiments the higher the SGO-T activity, the larger the infarct; for example, the SGO-T peak from a 0.5 g infarct was 64 units (24 above normal) and for an 18 g infarct 500 units.

The duration of abnormally increased but falling SGO-T activity was four to five days in animals with large infarcts, and 24 hours when smaller areas of infarction were produced. Thus, both the height and duration of increased enzyme activity appeared to be proportional to the size of the infarct. Analysis of the homogenates of the infarcted heart muscle showed a progressive decrease in GO-T activity with time which was proportional to the age of the infarct. Uninfarcted muscle from the same animal showed normal concentration of GO-T.

In similar experiments on seven dogs given 5 to 60 g infarctions the SGO-T activity increased three to ten times, the SGP-T three to five times and the SLD two to three times normal.[5]

(2) *Clinical:* Sera secured within 12 to 48 hours after the onset of unequivocal acute transmural myocardial infarction and daily thereafter in 300 patients have been analyzed for GO-T activity. In all but three instances when the serum was obtained at the time of acute infarction, the SGO-T activity rose two to 20 times normal within the first 48 hours (Fig. 2). The height and duration of increased SGO-T activity appeared to be roughly proportional to the size of the infarct as estimated electrocardiographically. Secondary elevations of SGO-T

were seen following recurrent chest pain due to extension of the infarction or the development of a new infarction in the same patient.

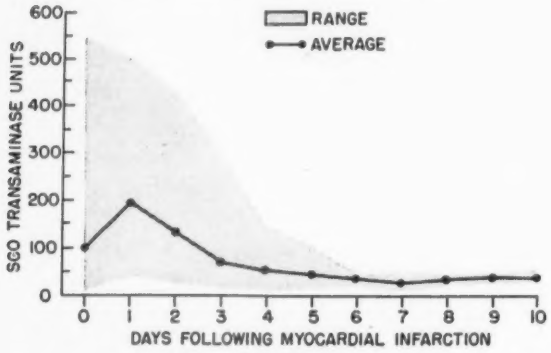

Fig. 2. The range (stippled area) and average (solid line) serum glutamic oxaloacetic transaminase activity following the onset of acute transmural myocardial infarction in 300 patients.

In ten patients with acute transmural myocardial infarction who had studies of the activity of all three enzymes, the SGO-T rose two to 20 times normal, the SLD two to ten times normal, and the SGP-T one to three times normal. The SLD activity remained elevated two to three days longer than the SGP-T activity[7,8] (Fig. 3).

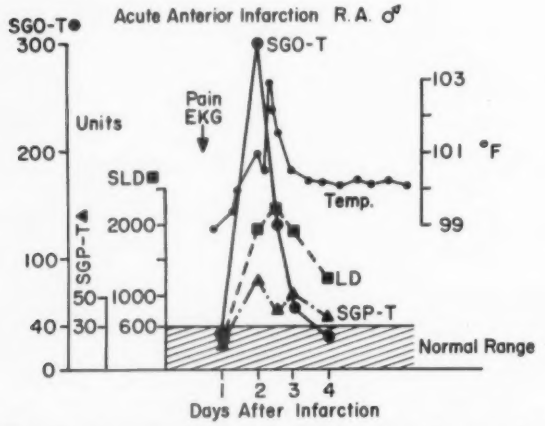

Fig. 3. A comparison of the average changes in serum glutamic oxaloacetic transaminase, serum lactic dehydrogenase and serum glutamic pyruvic transaminase activity in a case of acute transmural myocardial infarction.

When left bundle branch block obscured diagnostic electrocardiographic evidence of infarction in patients with severe chest pain, the SGO-T rose in some instances indicating the presence of acute myocardial necrosis, but in other instances no elevation occurred, suggesting the absence of infarction. The clinical course of these patients usually suggested that infarction was present when the transaminase was elevated. Four patients with electrocardiographic evidence compatible with subendocardial infarction were studied; in two, clear-cut increases in SGO-T activity occurred. The electrocardiograms in the other two patients reverted toward normal when digitalis was withdrawn. When the SGO-T was elevated in patients with equivocal electrocardiographic changes, the usual treatment for myocardial infarction was instituted. If the transaminase level was within normal limits, the patients were usually allowed out of bed within one week. These findings have been corroborated elsewhere.

No correlation has been found between the SGO-T activity and the white blood count, the sedimentation rate, the presence or absence of shock, the absolute levels of the blood pressure, the presence of heart failure, the location of the infarction, or the use of anticoagulant drugs. Peak activity above 350 units was associated with a marked increase in mortality rate.

There was also a significant correlation between the SGO-T activity and the electrocardiographically estimated size of the infarct. Higher enzyme levels were associated with more extensive electrocardiographic changes.

SGP-T activity increases proportionately less than SGO-T following injury to heart muscle but is more elevated following acute liver cell injury. SLD activity, however, is relatively unaffected by liver cell injury but rises following heart muscle or skeletal muscle damage in parallel fashion to SGO-T.

ANGINA PECTORIS AND CORONARY INSUFFICIENCY

Myocardial ischemia in 15 dogs was produced by lifting a ligature placed ten days previously under a coronary artery so as to cause marked T wave and ST segment changes but no Q wave changes. Four of these animals developed subendocardial infarction and all had elevated SGO-T activity. In the remaining eleven no microscopic evidence of heart muscle cell injury was found and the SGO-T activity remained within normal limits in all but one

dog despite the appearance of temporary electrocardiographic evidence of ischemia manifested by ST segment and T wave changes.

Angina pectoris of variable duration has not been followed by an increase in SGO-T activity. The SGO-T activity was studied in 50 patients with coronary insufficiency whose electrocardiograms showed evidence of ischemia as manifested by moderate to marked T wave inversion sometimes associated with ST segment changes but without Q wave abnormalities. The SGO-T activity remained within normal limits in 34 of these patients despite the persistence of prolonged substernal pain. The SGO-T activity rose in 16 of these patients suggesting acute heart muscle cell damage. In eight instances pain had been present for three to six days before the SGO-T increased[6] (Figs. 4, 5).

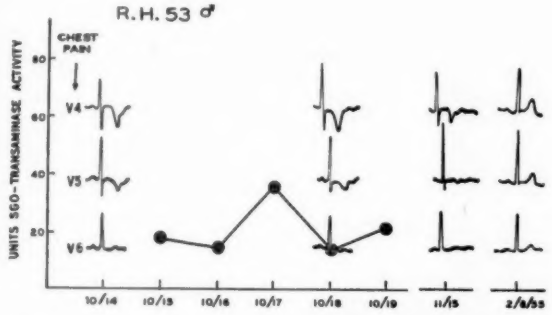

Fig. 4. Marked, reversible ECG abnormalities in a patient with incapacitating angina recurring every 30 minutes from 10/8 to 10/20. The serum glutamic oxaloacetic transaminase remained normal.

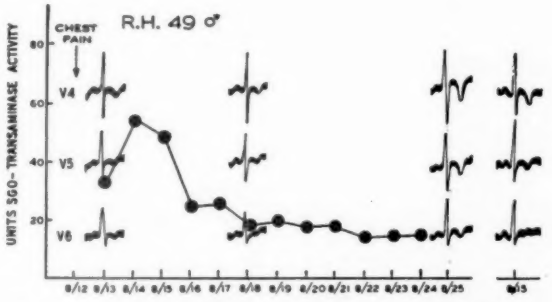

Fig. 5. Serum glutamic oxaloacetic transaminase elevation in a man who had similar chest pain and ECG changes, but an increased SGO-T activity.

ACUTE PERICARDITIS

The SGO-T was followed daily or oftener in 11 patients with unequivocal evidence of acute pericarditis of varying etiology and remained within normal limits in nine throughout the period of study. Two exhibited minor increases in SGO-T activity which were thought to be due to the presence of coexistent liver disease due in one instance to infectious mononucleosis and in the other to leukemia.[4]

RHEUMATIC CARDITIS

The SGO-T activity in acute rheumatic fever without carditis was not elevated. In some but not all patients with extensive rheumatic carditis the SGO-T activity was increased. It is to be noted that the administration of large doses of aspirin to children will also cause elevation of the SGO-T activity.[10]

PULMONARY INFARCTION

The SGO-T activity was followed during the course of pulmonary infarction in seven patients and remained at normal levels in all but one patient whose peak enzyme activity was 80 units.[9]

Discussion

Although the spectrophotometric method employing the Beckman DU spectrophotometer is the most rapid and accurate method for the analysis of SGO-T, SGP-T, and SLD, the Bausch and Lomb spectrophotometer using Steinberg's modified technic (for SGO-T) is more economical and practical for smaller laboratories. Colorimetric methods for all three enzymes have been devised and can be done using equipment already available in hospital laboratories. The serum should be separated promptly from the red blood cells avoiding hemolysis and then stored at refrigerator temperature for not more than four days. It is important to emphasize that *unless serum is received within three days after the onset of infarction, the SGO-T activity cannot be relied upon as evidence of acute myocardial damage.*

It is worth re-emphasizing that SGO-T activity is not increased as a result of infectious, degenerative, neoplastic, allergic, reactive, congenital diseases or pregnancy unless there is associated acute damage of heart muscle, skeletal muscle, liver, kidney, and brain. No consistent correlation has been found between the SGO-T

activity and the temperature, white blood count, sedimentation rate or CRP.

Although marked elevations of SGO-T activity are seen in hepatitis of varying etiology and moderate increases in some patients with cirrhosis and obstructive jaundice, the clinical setting is such that there is rarely any confusion in the differential diagnosis with acute myocardial infarction. Major surgery, when skeletal muscle is injured, is frequently followed by minimal to moderate increases in SGO-T, SGP-T, and SLD activity for one to six days which mimic those following acute myocardial infarction, so that measurements of enzyme levels postoperatively do not constitute evidence for or against the presence of acute heart muscle cell injury. Metastatic liver cancer, moderately severe hemolytic crises and mechanical injury to skeletal muscle are also associated with in-increased SGO-T activity.

Experimental and clinical myocardial infarction is followed by characteristic changes in the activity in SGO-T, SLD, and SGP-T with the peak activity occurring within 12 to 24 hours falling to or toward normal within two to five days. The height and duration of elevated SGO-T activity is roughly proportional to the amount of myocardial necrosis.

The SGO-T activity increases proportionately more than the SLD or SGP-T following acute human myocardial infarction. SLD can be measured by following the change of pyruvate to lactate which gives the maximum activity at physiologic pH or by measuring the changes from lactate to pyruvate at pH 9. Preliminary reports suggest the latter method gives results closely paralleling SGO-T, although the magnitude of SLD activity is five to ten times less by this method. It is of interest that the SLD activity persists two to three days longer than SGO-T activity following acute myocardial infarction.

SGO-T has proved particularly useful in deciding whether acute heart muscle cell damage has occurred when chest pain like that seen with myocardial infarction develops in patients with equivocal electrocardiographic changes. In such instances if the SGO-T is carefully followed throughout the duration of pain and for four to 12 days thereafter, many patients may be saved weeks of invalidism or anticoagulant therapy may be instituted to prevent impending infarction. Acute myocardial damage must be presumed to be present in patients with chest pain and equivocal electrocardiographic changes who have SGO-T elevation in the absence of known active liver disease. Further study is needed to evaluate the usefulness of SLD in such situations, remembering that minimal hemolysis will increase SLD activity.

Agress and co-workers found that most of their patients with SGO-T activity above 300 units did not survive their acute myocardial infarction.

The SGO-T activity will usually help distinguish acute pericarditis and pulmonary infarction from acute myocardial infarction, since SGO-T is uncommonly and only slightly and irregularly elevated following acute pericarditis and pulmonary infarction but rises promptly and follows a characteristic curve after acute myocardial infarction. Further study is needed to evaluate the significance of SGO-T alterations in acute rheumatic carditis.

The fact that infarcted heart muscle may contain one-fiftieth the GO-T, GP-T, and LD activity of normal heart muscle suggests that the increased levels in the serum following myocardial infarction result from the release of these enzymes from the damaged heart muscle cells in excess of that which the body can destroy or excrete.

Deviations in various enzyme elevations following tissue damage are not solely explicable on the basis of a simple release into the blood stream, and other mechanisms as yet unknown need to be elucidated.

Other enzymes present in heart muscle in high concentration may prove to be more significantly and more regularly elevated and remain so for a longer period of time than either SGO-T or SLD. It is obvious that continued study of other enzyme systems of many tissues or of tumors may provide useful information both with regard to diagnosis and changes in tissue cell metabolism.

The activity in the serum of phosphohexose isomerase was increased in 16 of 18 patients following acute myocardial infarction and that of

malic dehydrogenase in 17 of 18. The measurement of the activity of malic dehydrogenase, however, was admitted by the authors[11] not to be specific and until the technic is stabilized and more results available, the usefulness of these enzymes in the diagnosis of acute myocardial infarction is not established.

Nonspecific Phase Reactants: The nonspecific phase reactants, including the erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP), and fibrinogen, all have been studied as diagnostic aids in the diagnosis of acute myocardial infarction.[12, 13] It has long been known that the ESR becomes elevated within 12 to 24 hours after acute myocardial infarction and may remain elevated for as long as seven weeks. The increase in ESR following infectious diseases or any disease associated with inflammation is a well-known fact. However, all of these phase reactants are positive within the first three weeks in 90 to 98 per cent of patients sustaining acute myocardial infarction.

As intimated above, both the CRP and ESR and fibrinogen may be positive in infectious diseases as mild as an acute upper respiratory infection, in gastrointestinal diseases which are complicated by infection, in acute gout, in neoplastic diseases, as well as being altered by the mere presence of severe congestive heart failure. They are also strongly positive following pulmonary infarction, and of course in pericarditis and acute rheumatic fever and rheumatoid arthritis and collagen diseases.

Recent reports have shown that in almost 100 per cent of patients sustaining an acute transmural myocardial infarction the CRP is positive after the third day.[14, 15] The test for CRP remains positive for as long as three to seven weeks, although it is usually elevated for only two weeks in the absence of complications. Certainly the CRP returns to normal before the ESR in most instances. The CRP has proved to be negative in patients with acute coronary insufficiency, whereas the sedimentation rate may be elevated in some instances. These tests have the advantage of simplicity and adaptability to most laboratories but must be evaluated carefully because of their lack of specificity and abnormal values in a wide range of disease states.

The CRP is of particular value when blood samples are not obtained within the first four days following myocardial infarction since CRP remains positive much longer than does the SGO-T. The investigators who have studied the CRP have stated that this test may uncover small infarctions when the transaminase is normal. However, such findings must be carefully evaluated in the light of the nonspecificity of this reaction.

Conclusions

(1) SGO-T, SLD and SGP-T activity in the absence of acute damage of heart or skeletal muscle or of liver has been found to be within normal limits in the following types of disease: infectious, degenerative, neoplastic, toxic, allergic, reactive, and metabolic.

(2) SGO-T, SLD and SGP-T activity rises within 12 hours and persists as long as six days after acute transmural myocardial infarction.

(3) The height and duration of elevation of SGO-T, SLD, and SGP-T are roughly proportional to the size of infarction.

(4) Angina pectoris or coronary insufficiency is not associated with a rise in SGO-T, SLD, and SGP-T activity unless, presumably, accompanied by heart muscle cell damage.

(5) Rheumatic fever with active carditis is frequently associated with concomitant increases in SGO-T activity.

(6) The ESR rises within 12 to 24 hours after acute myocardial infarction and may remain elevated for as long as seven weeks. Unfortunately, this modality also becomes abnormal with coronary insufficiency without infarction.

(7) C-reactive protein is also positive in nearly 100 per cent of patients after the third day of acute myocardial infarction and remains elevated for as long as three to seven weeks.

(8) Blood fibrinogen level reacts similarly to the C-reactive protein.

(9) All of these nonspecific phase reactants including the ESR, the CRP and fibrinogen are strongly positive following many infectious disease processes, neoplastic diseases, gout, some gastrointestinal disorders, pulmonary infarctions, arthritis, and acute rheumatic fever to mention a few. Therefore, changes in the phase reactants must be carefully evaluated

when used as a diagnostic aid for acute myocardial infarction.

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Diagnosis of Atherosclerosis

I. Correlation Between Clinical Diagnosis, Serum Cholesterol and Low-Density Lipoproteins, and Resting and Exercise Electrocardiograms

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ONE OF THE significant advances in medical practice is the growing recognition by the profession that atherosclerosis is a disease and therefore probably susceptible to prevention and therapy. Abnormalities of lipid metabolism have thus far been the focal point of attention since they are etiologically important, and various approaches afford considerable promise in correcting the usually elevated serum lipids. The rapidly accumulating evidence in this area has recently been summarized.[1–3] When atherosclerosis is far advanced, the diagnosis usually presents no problem, but in these cases prophylaxis and therapy are least beneficial. They are most efficient when instituted early in the disease, the stage at which diagnosis is difficult and uncertain. Various procedures have been advocated as useful in the earlier recognition of atherosclerotic disease, or of a predisposition to it. Among these are electrocardiograms after exercise, ballistocardiograms, vectorcardiograms, lateral x-rays of the abdominal aorta, and serum cholesterol and lipoprotein measurements. There is considerable disagreement among investigators as to the significance of the various instrumental findings, and of the different lipid and lipoprotein determinations. It may be that few definitely positive or negative early diagnostic criteria will be found. However, if any of the tests, singly or in combination, can define a lesser or greater probability of atherosclerotic disease before it is far advanced, preventive measures can be most effectively applied.

During the past five to six years combinations of some of the laboratory tests suggested in the recognition of atherosclerosis were performed in 560 adult patients* in private practice. These tests included serum cholesterol and ultracentrifugal lipoprotein analysis, and electrocardiograms and ballistocardiograms at rest and after a double two-step exercise test (except where known previous myocardial infarction had occurred). Evaluation of the electrocardiograms and ballistocardiograms was recorded on the chart by the author before the results of the lipid determinations were known. Although the subjects were not scrutinized with all the finer technics found only in research institutions, this series does possess the advantage of having the same examiner for the entire group, the use of modalities available in a private office, and a patient population fairly representative of that seen in the practice of internal medicine. Given these circumstances, it seemed desirable to study some of the relationships demonstrated between the clinical diagnosis and the various laboratory tests. The observations involving both lipid tests in this independent series were particularly important in view of the differences between two expert groups of observers[4] as to the prognostic significance of serum cholesterol and lipoprotein determinations.

* No patients were included in this series who had been on restricted diets or who were taking medication such as thyroid which might have influenced serum lipid levels.

Procedure

The patients were usually seen in the afternoon and the various tests performed after the history and physical examination were completed. Thus, at least one hour had elapsed after the previous meal. The electrocardiograms and ballistocardiograms were taken with the subject lying on a rigid wooden platform. The electrocardiogram consisted of the standard and augmented limb leads and six precordial V leads. The ballistocardiogram was of the displacement type taken at the mid-tibial area. Although more discriminating office ballistocardiographic instruments are now available, the same machine was used throughout this study since it gave satisfactory, fairly reproducible records and the data were therefore comparable over the five-year period of study.

If the resting electrocardiogram was normal, and no symptoms of cardiac disease were present, a double two-step test following Master's criteria[5] was then performed, and the electrocardiogram taken after exercise followed by the ballistocardiogram. The precordial leads were then taken again. No exercise test was done if a history of definite prior myocardial infarction existed. When symptoms of possible ischemic heart disease were present, the single two-step test was performed initially, and the double two-step test was subsequently done only if the shorter exercise procedure did not result in an abnormal electrocardiogram. Blood was then drawn for the lipid determinations. Serum was analyzed for cholesterol in the office laboratory by the same method throughout the study,[6] and aliquots were mailed for ultracentrifugal determinations of low-density lipoproteins.*

The two lipid parameters were determined independently. No clinical data other than weight, age, and sex were supplied to the laboratory performing the ultracentrifugal analyses. The author's interpretation of the resting and exercise electrocardiogram and ballistocardiogram was recorded on the chart prior to the determination of the lipid values. Thus, from the standpoint of the relationships between the clinical diagnosis and lipid tests on the one hand and between the latter and cardiac tests on the other, blind study technics were applied. Changes in post-exercise electrocardiograms were described rather than classified as positive or negative, as there is some disagreement about the importance of lesser S-T segment and T wave changes after exercise. The ballistocardiographic findings† will be presented in a separate report.

TABLE I

Cholesterol and Atherogenic Index Values in Male and Female Normals and in Those with Prior Myocardial Infarction

		21 to 40 yr		41 to 50 yr		51 to 60 yr		61 and over	
		M	F	M	F	M	F	M	F
Myocardial infarction	Cholesterol	305	449	331	507	296	434	288	339
	Atherogenic index	123	130	116	119	111	119	106	121
Number of cases		8	1	44	14	34	13	17	18
Normal	Cholesterol	259	276	284	260	272	291	288	263
	Atherogenic index	94	65	92	61	89	87	83	68
Number of cases		71	14	112	30	50	33	27	12

Findings and Comment

The average serum cholesterol and low-density lipoprotein values in 149 individuals with a history of old myocardial infarction, and in the 349 persons with no clinical evidence of severe coronary, peripheral or cerebral atherosclerotic disease, are presented in Table I.

* Performed at the Institute of Medical Physics, Belmont, California.

† Diagnosis of Atherosclerosis. II. Correlation Between Serum Cholesterol and Low Density Lipoproteins, and Resting and Exercise Ballistocardiograms (to be published).

Lipoprotein levels are shown as atherogenic index values (A.I.), which are figures based upon the actual quantity of Standard Sf 0–12 and 12–400 lipoproteins.[4]

Sex Differences: The male to female ratio was 103 : 46 in the coronary group and 260 : 89 in the normal group. Several interesting facts are apparent from the data. In the normal group up to 50 years of age there is no difference between the sexes in serum cholesterol, whereas the atherogenic index is significantly lower ($p<0.01$) in females. Thus, up to the menopause, the lipoprotein determination parallels the known sex differentiation in the incidence of coronary disease and the measurement of serum cholesterol does not. This fact, previously noted,[8] has been insufficiently stressed since it alone is good evidence of the superiority of lipoprotein over cholesterol analysis in indicating the probable presence of atherogenesis up to 50 years of age.

Age Differences: Cholesterol levels in normal males seem to follow no particular pattern with age in this series, but the atherogenic index shows a gradual decrease with increasing age. In normal females, after the post-menopausal sharp increase in both lipid values, but more significantly in the lipoproteins, there is a decline in both parameters in the oldest group. In males with myocardial infarcts lipoprotein values are significantly higher ($p=0.01$) at all ages than in corresponding normal males, but cholesterol levels are the same in both groups above 60 years of age and are barely statistically significantly elevated ($p=0.05$) in the 51 to 60 age category. In the female infarct group a surprisingly large proportion (15 : 46) of the total was under 50 years of age. In all the female coronary patients both lipid measurements were significantly different from the corresponding normal groups. Among the male coronary cases particularly, it is apparent that the higher the lipoprotein levels the earlier the infarction. This is also probably true of cholesterol, but the relationship is not as clear. Since the total individual data were too voluminous to present, it should be stated that the average values disguised the fact that there were normal individuals above 60 years of age with high lipid values, and some younger coronaries with normal lipids. These were exceptions, however, to the general findings so clearly demonstrated in Table I.

Peripheral Atherosclerosis: There were 27 patients in the group whose presenting complaint was referable to peripheral sclerotic disease, who had no obvious severe coronary disease or in whom the symptoms of myocardial ischemia appeared only subsequently. Lipid findings in this small group are shown in Table II. Both the average cholesterol and atherogenic index were markedly elevated. However, there were several patients with much lower values. The findings in this small series differ from those recently reported[9] in a group of diabetic patients with peripheral vascular disease. It is interesting that two of the three individuals below the age of fifty had blocking at the lower aortic-iliac area (Leriche syndrome) and that the lipid levels were extremely high in these individuals. It would therefore be desirable to measure the serum lipids after surgical resection of segmental aortic-iliac blocks in order to apply preventive lipid-lowering measures where indicated. This is particularly true where vascular grafts have been used, as recent evidence in animals has shown that such tissue becomes infiltrated with fat and cholesterol when the serum is hyperlipemic more quickly than the normal vascular tree.

TABLE II

Cholesterol and Atherogenic Index Levels in Patients with Symptoms of Peripheral Arteriosclerotic Disease as the Initial Complaint

	Below 50 years*	Above 50 years
Cholesterol	406	347
Atherogenic index	184	111
Number of cases	3	24

* Two of the three patients had a block at the lower aortic-iliac area.

Hypertension: There were 100 patients with hypertension (above 160/100) in the entire group. Their average cholesterol and lipo-

protein levels are shown in Table III arranged according to age and to the presence of coronary or cerebral complications. The role of elevated lipid levels in contributing to vascular disease in hypertensives is clearly indicated by the data. The highest lipoprotein values were found in younger hypertensives who had had an acute myocardial infarction or a cerebrovascular accident, whereas the serum cholesterol and low-density lipoproteins of older, uncomplicated hypertensives are at normal levels. The differences in both cholesterol and atherogenic index between the complicated and uncomplicated groups at all ages are significant, very highly so, above the age of fifty. These findings are in agreement with those reported earlier for Sf 10–20 levels in hypertensives.[10] Animal experiments have also shown that when the blood pressure is quite high and the blood cholesterol is not elevated, atheromata do not develop, but when hypercholesterolemia is present even a small rise in blood pressure greatly increases atheroma formation.[11] Several practical conclusions can be drawn from these facts. It is particularly important to measure serum lipids in individuals with hypertension since they are in double jeopardy if the lipids are also elevated. From the prophylactic standpoint both elevated blood pressure and lipids should be reduced as early as possible.

Serum Cholesterol vs. Atherogenic Index: It is apparent from Table I that in this series the serum cholesterol and atherogenic index paralleled each other in being significantly elevated in the coronary group except for the superiority of the atherogenic index in males above 50 years of age. There has been considerable disagreement on this point,[4] and follow-up studies over more extended periods of time are needed. The data in Tables IV and V may help to clarify the relative accuracy of the two lipid parameters as indicators of atherogenesis. There were 23 individuals out of the 149 patients with definite myocardial infarction in whom either or both values were low. The findings are shown in Table IV. In seven cases both lipid measurements were not elevated.* In nine of the 149 coronary cases the atherogenic index was below 90, and in only three of these was the cholesterol above 250, in only two above 280. Conversely, in 18 of the 149 coronary cases the cholesterol was less than 250, and in 12 of these the atherogenic index was above 90. A "normal" cholesterol was thus

TABLE III

Lipid Values in Hypertensive Patients with and without Cardiac or Cerebral Complications

Age Range		No complications			Complications			Difference between means	SE
			MD	SD		MD	SD		
Below 50	Cholesterol	275	58	71	323	48	56	48	23
	Atherogenic index	88	41	72	124	19	23	36	16
	Number of cases	24			12				
Above 50	Cholesterol	264	37	41	321	55	67	57	9.1
	Atherogenic index	75	19	26	105	20	26	30	6.6
	Number of cases	30			34				

MD = Mean deviation
SD = Standard deviation
SE = Standard error of the difference between means

* The upper limit of "normality" of serum cholesterol and of lipoproteins has not been accurately defined.

TABLE IV

Cholesterol and Lipoprotein Levels in 23 Patients with Definite Coronary Disease in Whom Either or Both Lipid Parameters Were Low

Sex	Age	Cholesterol	Atherogenic index	Sex	Age	Cholesterol	Atherogenic index
M	43	247	122	M	67	233	99
M	54	253	77	M	64	210	67
M	48	241	95	M	52	241	81
M	52	202	73	M	65	246	55
F	58	219	51	M	64	193	47
F	61	235	96	M	66	241	121
M	62	241	99	M	63	244	123
M	64	296	74	M	68	227	108
M	62	230	93	F	51	200	110
M	54	293	66	M	42	265	109
F	29	244	136	M	47	253	109
M	37	213	141				

found in 12 per cent, a "normal" lipoprotein analysis in only 6 per cent. It is apparent that serum cholesterol failed more frequently to indicate the probability of coronary disease in known infarction cases than the atherogenic index. The corollary analysis, seen in Table V,

TABLE V

Cholesterol and Atherogenic Index Levels in 16 Clinically and Electrocardiographically Normal Individuals 60 Years of Age and Over in Whom Either or Both Lipid Parameters Were Elevated

Sex	Cholesterol	Atherogenic index	Sex	Cholesterol	Atherogenic index
M	305	75	M	335	102
M	312	71	F	365	99
M	350	115	M	340	89
F	355	74	M	355	96
M	301	108	M	390	98
M	397	102	M	379	93
M	299	109	M	360	66
M	350	98	M	272	112

shows values in clinically and electrocardiographically (at rest and after exercise) normal individuals over 60 years of age in whom either or both lipid parameters were elevated. In eleven the serum cholesterol was above 250 and the atherogenic index was above 90. In five cases the cholesterol level was over 280, but the atherogenic index was below 90. In no instance when the atherogenic index was above 90 was the cholesterol below 250. Thus, in apparently normal elderly individuals, when the two lipid measurements were not in agreement with each other, serum cholesterol failed more frequently to indicate the clinical situation correctly. In summary, although cholesterol and low-density lipoprotein determinations are usually parallel, there are more false positives and false negatives using cholesterol as an index of atherosclerotic disease than when the atherogenic index is applied.

Correlation of Blood Lipids and Electrocardiogram: Table VI shows the average cholesterol and lipoprotein levels in patients with known previous infarction or those in whom the electrocardiogram showed changes of myocardial ischemia at rest or after the double two-step test. To the author's knowledge studies of correlations between circulating lipids and the electrocardiographic findings after exercise have not previously been presented. Both lipid determinations are not significantly elevated above control levels when the post-exercise change was a 0.5 mm S-T segment depression, or a flat or inverted T wave alone. In the patients with a 1 mm S-T segment depression the atherogenic index was elevated, but a statistically

TABLE VI

Cholesterol and Atherogenic Index Values in Subjects with Various ECG Changes at Rest and After a Double Two-Step Test

	ECG changes after double two-step test. Normal resting ECG							Abnormal resting ECG	
	No change	0.5 mm ST segment drop	Flat or inverted T waves	0.5 mm ST sag + flat or inverted T waves	1 mm ST segment drop	1 mm ST sag + flat or inverted T waves	2 mm ST segment drop	Flat or inverted T waves	Old infarct
Cholesterol	279	278	263	341	282	294	303	332	344
Atherogenic index	84	89	89	119	96	126	103	109	115
Number of cases	270	43	17	5	16	2	32	26	149

significant difference could not be established. In seven individuals who showed the combination of a 0.5−1 mm S-T segment depression plus T wave changes, the lipid values were significantly raised. When a 2 mm S-T segment drop occurred after exercise, with or without associated T wave changes, the lipid values were significantly higher. They were even more elevated in individuals with an abnormal electrocardiogram at rest, or a known prior myocardial infarction.

Although the presence of hyperlipidemia certainly does not prove the existence of advanced coronary atherosclerosis, one would anticipate, in a series in which known cases of coronary disease had significantly higher lipid values than normal individuals, that patients with electrocardiographic changes truly indicative of coronary narrowing would have an average elevation of serum lipids. No significant elevation was found in the values of those patients who had only 0.5 mm S-T segment depression or flat or inverted T waves after exercise, a finding in agreement with the general clinical impression that these variations may be within normal limits. When both these minor changes occurred in the same record, marked* hypercholesterolemia and hyperlipoproteinemia were present, suggesting that the combination of two minor electrocardiographic changes after exercise was more significant than either alone. When a 1 mm S-T segment depression occurred after exercise, the average atherogenic index was elevated but not significantly so, perhaps because of the small number of cases. When a marked post-exercise change occurred, a 2 mm or more S-T segment depression with or without T wave changes, both lipid values were raised. In the category of abnormal electrocardiograms at rest, generally indicative of more severe disease than when exercise is required to establish a diagnosis, lipid levels were still higher.

* These levels may be excessively high because of the inclusion of two patients in this category who had very elevated cholesterol and lipoprotein values.

Discussion

In this study an attempt was made to probe the relationships of some of the tests which have been suggested for the earlier recognition of the atherosclerotic tendency and of atherosclerotic disease. The latter is essential for the more efficient application of preventive medicine in the adult years. In the area of early diagnosis the physician must be extremely careful not to incite fear and concern needlessly, but at the same time failure to recognize threatening serious illness is not good medicine. This is particularly true now that so much more can be done to correct fat metabolic abnormalities than in former years.

The finding in this series of patients of a substantial direct correlation between elevated circulating lipids, anoxic electrocardiographic

abnormalities at rest and after exercise, and ballistocardiographic abnormalities at rest in younger individuals and after exercise at all ages (to be presented as a separate report, see footnote page 316, indicates the general relationship which exists among these various tests. Regardless of recently published[4] disagreements as to the relative advantages of cholesterol or lipoprotein determinations in the prognosis of coronary disease (a confusing situation which could perhaps have been avoided by a longer period of observation of the subject population) all the available evidence indicates that lipid elevation precedes the development of atherosclerosis. Thus without exception in all animal species blood cholesterol and lipoprotein must be increased before atherosclerosis occurs. This does not imply that elevated lipids always mean that atherosclerotic disease is present. In this series the serum cholesterol and the atherogenic index were usually parallel. However, certain facts indicated that the latter is superior to cholesterol as an indicator of the tendency to develop atherosclerosis. In pre-menopausal women the serum cholesterol was essentially at the same level as in males, whereas the low density lipoproteins were much higher in the men. It is a well-documented fact that atherosclerosis occurs much more frequently in young males than in young females. In the known cases of infarction the cholesterol was below 250 mg in 12 per cent, the atherogenic index was below ninety in only 6 per cent. Also, in clinically and electrocardiographically normal elderly patients cholesterol was more frequently elevated than the lipoproteins. Perhaps of greater importance in a practical sense, however, was the recent finding that various areas of the lipoprotein spectrum are affected differently by fat or carbohydrate alterations in the diet.[11] Thus when diets were kept isocaloric, a restricted animal fat intake lowered the Sf 0–20 lipoproteins, whereas the Sf 20-400 lipoproteins were more responsive to changes in the carbohydrate content of the diet. It is therefore apparent that the ultracentrifugal lipoprotein analysis will give more information to the physician as a guide to dietotherapy than cholesterol or electrophoretic lipoprotein measurements.

The usefulness of the exercise tolerance test and post-exercise electrocardiography in the differential diagnosis of chest pain is well established. However, the exercise procedure is far less widely applied in the work-up of the asymptomatic adult. This is difficult to understand since a normal resting electrocardiogram is so frequently found in the presence of known coronary disease. It has been shown that an S-T segment depression after exercise in excess of 0.5 mm in clinically normal individuals was the best prognostic criterion of coronary insufficiency.[12] This fits in well with the evidence just presented that the more marked electrocardiographic changes after exercise are associated with elevated lipids. Furthermore, in our series, some of the patients with more significant post-exercise changes than an 0.5 mm S-T segment depression alone had no clinical symptoms referable to myocardial ischemia. These findings strongly indicate the desirability of adopting the double two-step electrocardiogram as a routine diagnostic measure in the cardiac evaluation of clinically normal individuals.

It may reasonably be argued that cholesterol and lipoprotein analysis should be performed in all adults in order to detect those individuals most likely to develop atherosclerosis. While this point of view has much to recommend it, the cost of the tests is considerable. Furthermore, there is a small percentage of patients with clinical disease and low lipids, and some individuals of advanced age with no detectable disease and elevated fats.

The patency of the coronary or peripheral arteries is not defined by blood chemistry determinations. Since the clinician is concerned about the extent of disease, and should be equally alert about its likelihood, all the modalities discussed should be applied. The positive relationship found in this study between elevated lipid and lipoprotein levels and electrocardiographic evidence of myocardial ischemia after exercise substantiates the validity of the combined diagnostic approach. This will frequently aid in the earlier diagnosis of atherosclerotic involvement so that prophylactic measures may be applied more effectively.

Summary

(1) The electrocardiographic findings at rest and after exercise, serum cholesterol, and ultracentrifugal lipoprotein analyses (atherogenic index) have been presented in a series of 560 adult private patients.

(2) In normal individuals up to the age of fifty serum cholesterol did not differ significantly between the sexes whereas the atherogenic index was significantly lower in females, thus paralleling the known lower incidence of atherosclerosis in pre-menopausal women.

(3) Patients who had experienced a myocardial infarction had significantly elevated lipid levels at all ages.

(4) Although the cholesterol and atherogenic index values were usually parallel, when the lipid parameters were divergent the lipoprotein determination was the more accurate of the two as related to the clinical diagnosis.

(5) The serum cholesterol and lipoproteins were high in 27 patients in whom peripheral atherosclerotic disease was the presenting illness.

(6) In 100 patients with hypertension, the average lipid values were significantly elevated in those individuals who had experienced a coronary or cerebral incident.

(7) The lipid measurements correlated directly and significantly with the severity of the electrocardiographic findings at rest and after exercise.

(8) The combined application of the various modalities is useful in the earlier diagnosis of atherosclerotic disease, and in the selective application of prophylactic measures.

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Ultra-Low Frequency Acceleration (Force) Ballistocardiogram in Myocardial Infarction*

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ANALYSIS of the acceleration (force) ballistocardiogram in 30 subjects with proven myocardial infarction recorded on the ultra-low frequency system described by Rappaport[1] has revealed a rather high incidence of one specific type of abnormal pattern. This pattern has not been noted in any of 138 subjects with other forms of heart disease or with normal hearts.

METHOD

The ultra-low frequency pendulum bed used in this laboratory is designed and patterned after that of Rappaport.[1] It has been in use for some two and one-half years at this writing (May 1957). Because there are some differences it is described in detail.

Figure 1 illustrates the very light weight pendulum bed made of aluminum frame ($1^1/_2$ in. tubular), 2 x $6^1/_2$ feet and covered with nylon airplane cloth. It is suspended from the ceiling by four cables, each ten feet long. The cables are wrapped with adhesive tape to reduce high frequency cable vibration (about 40 cps). Two small steel-hardened cups are attached to one side of the aluminum frame about one foot from the ends. Another pair of cups is attached to an adjustable crank on a heavy wooden frame resting on the floor. Highly polished hardened steel pins with rounded ends (7 cm x 3.5 mm) are positioned in these cups, allowing the bed to be displaced away from the null position as desired. The bed, including two cups, hooks for cable attachment and transducer, weighs just under eight pounds.

The bed, as utilized, is completely undamped. The natural frequency in the free position is 0.35 cps. Utilizing the Henderson pins, displacement of the bed 2 cm from the null reduces the frequency to 0.25 cps, and a displacement of 7 cm to less than 0.2 cps.

The use of a bar magnet velocity meter as a sensing device and differentiation to acceleration by an electrical circuit proved unsuitable because of electrical interference and building vibration.[7] The frequency and amplitude of these were such as to obscure the tracing.

We have chosen to record the ballistocardiographic tracings in terms of acceleration to obtain the closest approximation of a force tracing.[1,6] The transducer, an accelerometer of the variable reluctance type,† is mounted at the foot end of the frame. It is sensitive to changes in acceleration only, recording zero amplitude when no acceleration change occurs. Essentially, it is sensitive to change only in the long axis or the head-foot direction. The sensitivity in any direction 90° away from this axis is about 1 per cent and falls off very rapidly a few degrees from the longitudinal axis. The natural frequency of the transducer is 180 cps, and full scale is 0.25G. Damping is set at 30% of critical for better high frequency response when used with the Polyviso recorder. Recordings are made on a Sanborn Polyviso recorder through a strain gauge amplifier.

The ballistocardiogram is recorded simultaneously with lead 1 or 2 of the electrocardiogram, a low frequency phonocardiogram, and carotid pulse tracing. The accelerometer is calibrated so that one chart mm amplitude represents 3.5 mm per second per second of acceleration.

Calibration is determined by displacing the bed 1 or 2 cm from the null utilizing a thread attached to the frame. The bed is allowed to swing by burning the thread with a match flame. The recorder is run at 50 mm per second and the amplitude measured for the first few cycles. Acceleration is determined by the formula $A = \frac{4\pi^2 X}{T^2}$ where X = displacement and T = period.

The principles and advantages of the ultra-low frequency system have been adequately described and discussed.[6]

MATERIAL

One hundred sixty-eight subjects have been

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† Pace Engineering Co., North Hollywood, California.

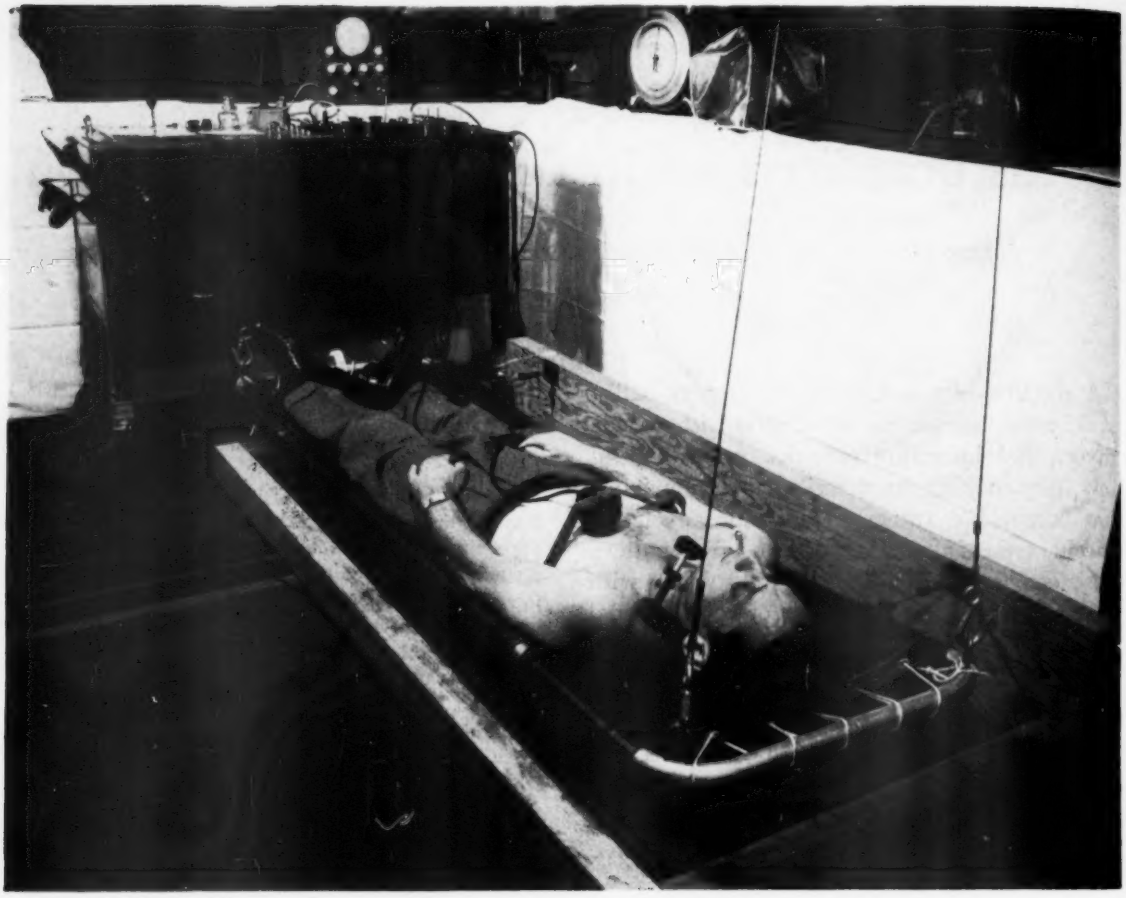

Fig. 1. The ultra-low frequency pendulum bed used in the Cardiopulmonary Laboratory of the Cedars of Lebanon Hospital.

TABLE I
Sex Distribution

Male	97
Female	71
Total	168

TABLE II
Age Distribution

1–9	5
10–19	4
20–29	28
30–39	26
40–49	37
50–59	34
60–69	25
70–80	8
83	1

studied through May, 1956. Tables I, II and III indicate respectively the sex, age and etiologic distribution. All subjects underwent complete history and physical examinations, routine blood count and urinalysis, chest x-ray and/or cardiac fluoroscopy, electrocardiogram and spatial vectorcardiogram. Forty-three subjects underwent cardiac catheterization in this laboratory. Recordings were made during quiet respiration, suspended inspiration and suspended expiration.

Historical Background

Starr and Wood[2] utilizing the high frequency bed, have recorded four types of abnormal ballistocardiograms in post-infarction states: the early M pattern (large H wave), the late M pattern (the large L wave), the late downstroke pattern (small H, I and J, and a deep K

TABLE III

Etiologic Classification

Normal subjects		44
Congenital heart disease		14
Rheumatic heart disease		40
Mitral disease	24	
Aortic disease	8	
Combined valvular disease	8	
Atherosclerotic heart disease		61
Complete A-V block	6	
Angina	3	
Congestive heart failure	5	
Myocardial infarction	47*	
Miscellaneous		9
Undiagnosed	5	
Pericarditis	1	
Emphysema	1	
Hiatus hernia	2	
Total		168

* 30 of these with clinical or objective confirmation were utilized in this presentation.

wave) and a grade four pattern without distinguishable waves. The latter was most frequent.

Brown, *et al.*[3] with similar technics, have reported identical abnormalities and add that the earliest abnormality found is a marked increase in the respiratory variation between the large and the small complexes.

Mandelbaum and his group[4] agree with both Starr and Brown, and in addition have noted many fusion waves, excessive notching, and particularly low amplitudes among the H, I and J waves. Smith and Rosenbaum[5] have reported marked notching in the J and K waves in their acceleration tracings.

Results

Normal tracings have been found in all age groups from the first through the sixth decades. There is no qualitative sex difference, and the tracings are similar in appearance to those recorded by investigators using other ultra-low frequency methods of recording.[1c,6c]

The timing of the component waves (Fig. 7) is precise and in full agreement with that described by Rappaport.[1] The wave labeled J'' appears to be more widely separated from the J peak than depicted by Rappaport.[1] As in all methods of ultra-low frequency recordings the normal tracing is readily recognized and easily differentiated from the abnormal.

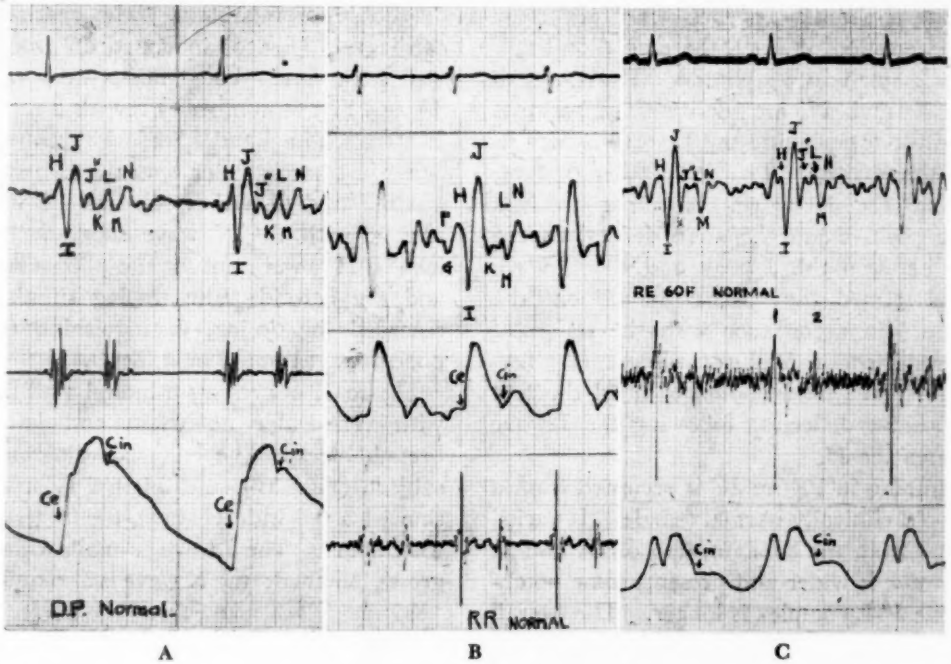

Fig. 2. Normal ultra-low frequency tracings: (A) normal female, aged 28; (B) normal female, aged 24; (C) normal female, aged 60. The tracings have been partially retouched.

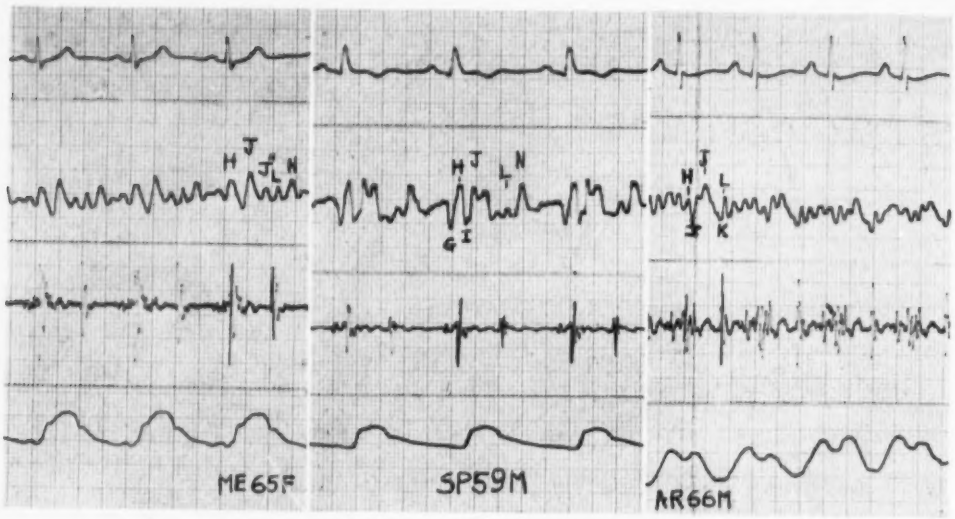

Fig. 3, A, B, C. Ultra-low frequency ballistocardiograms in myocardial infarction. The tracings have been retouched for clarity.

Figure 2 illustrates the normal ultra-low frequency acceleration ballistocardiogram, (A) and (B) in the early decades, and (C) in the sixth. All waves are sharply peaked with a minimum of notching. The major complex is the IJ wave. There is a small F and G wave, a sharply peaked narrow H about one-half the amplitude of the J. The J is sharp and clear with a suggestion of J′ on the ascending limb, and a J″, small in amplitude. The diastolic waves M and N are definite. A distinct negative wave preceding the L wave is seen in some of the tracings. This wave, when present, is labeled the K wave. In other tracings variable positive and negative deflections are present between the J peak and the L wave which is termed the "J-L segment" or "the K region," in accordance with the report of the Committee on Ballistocardiographic Terminology.[8] We have chosen to label the first major positive deflection following the J wave in this area the J″.

The tracing in Figure 2C is recorded from a 60-year-old clinically normal female. It varied somewhat from the configuration of 2A and B. The H wave is wider and presents some notching. The J″-L complex is longer. The overall configuration however is within normal limits.

Figure 3 illustrates tracings from three subjects with proven myocardial infarction. All were ambulatory when the tracings were made. The subject in Figure 3A was found in the "normal" group from the Surgical Service, having been hospitalized for breast surgery. Her electrocardiogram was considered to be within normal limits by the usual pattern method of interpretation (Fig. 4) and not diagnostic of infarction. The spatial vectorcardiogram (Fig. 5) indicated an antero-septal wall infarction. The ballistocardiogram (Fig. 3A and Fig. 6, number 6) reveals a rather wide H wave with a J and J″ of low amplitude, the J being just barely taller than the H wave. The small F and G and small diastolic waves are present with the N wave suggestively prominent. If it were not for the phonocardiogram and the carotid pulse tracing simultaneously recorded for timing, distinguishing the component waves would be difficult.

Figure 3B represents a lateral wall infarction with ventricular aneurysm and left bundle branch block. The ballistocardiogram of this subject (Fig. 3B) and Figure 6, number 7) showed a tall wide H wave, the largest wave of the tracing. The J wave is small, widened and grossly notched; the N wave is also quite tall.

Figure 3C is taken from the subject with a posterior wall infarction, a spatial vectorcardiogram indicating involvement of the diaphragmatic surface. The ballistocardiogram

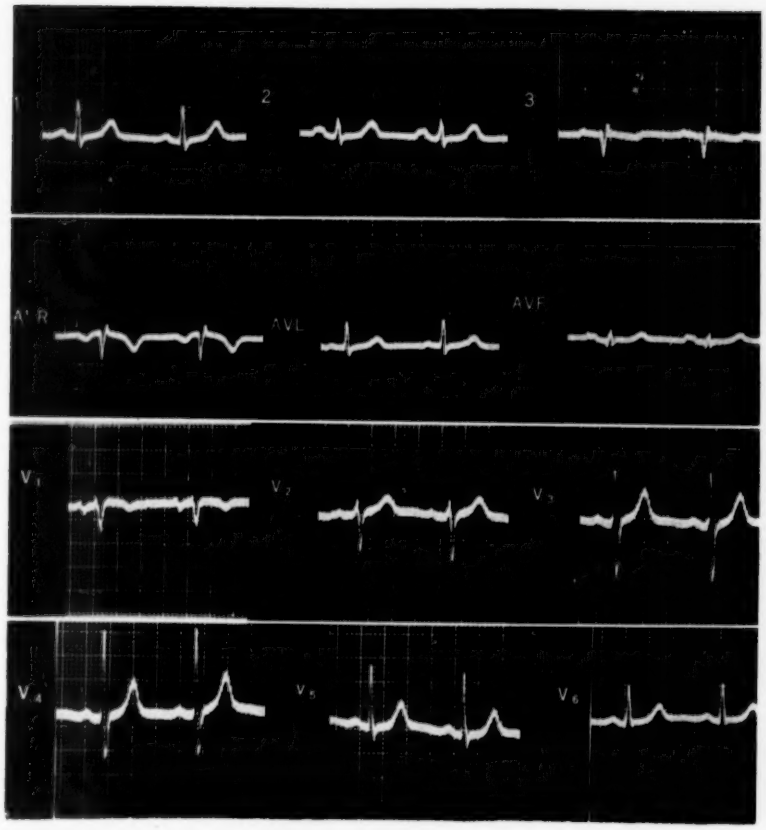

Fig. 4. ME, 65F. Electrocardiogram considered to be normal (by the usual pattern method of interpretation) and not diagnostic of infarction. Same patient as in Fig. 3A.

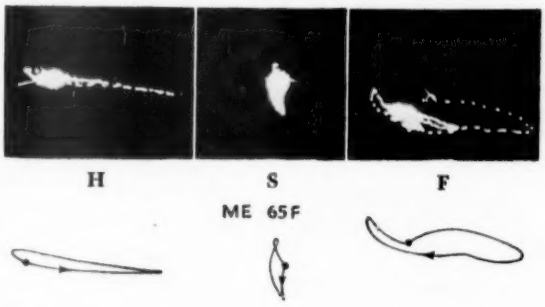

Fig. 5. ME, 65F. Same patient as in Figures 3A and 4. Spatial vectorcardiogram (Grishman Cube System) showing anterior septal myocardial infarction.

(Fig. 3C and Fig. 6, number 24) presents a series of clearly defined jiggles. All waves are small and abnormal.

In comparing these three infarction tracings with the normal presented above, the gross differences are readily apparent.

Figure 6 shows a representative complex from each of the 30 subjects who had sustained myocardial infarction. The electrocardiographic interpretation of myocardial infarction was made in 16 or 70 per cent of the series. Four patients had no electrocardiogram. The spatial vectorcardiogram by the Grishman Lead System, was interpreted as positive for myocardial infarction in 100 per cent of the 26 cases, four having had no spatial VCG. These figures represent the findings from a single tracing or a single VCG taken at the time of the ballistocardiogram. Making use of the information obtained from both the electrocardiogram and the spatial vectorcardiogram, the diagnosis of myocardial infarction was possible in all the cases studied.

Table IV describes each of the ballistocardiographic tracings from these 30 subjects. The tracings are grouped into three separate

TABLE IV

Description of Ballistocardiograph Waves of Figure 6

	Case	H	I-J	LMN	Pattern
Group I	1. GC	tall wide greater than J	small wide low J	prominent L and N	M
	2. JB	wide coarsely notched	wide notched J		M
	3. HS	tall wide notched slightly less than J	small wide notched J		M
	4. HD	tall greater than J	deep I, wide notched J	prominent N	M
	5. MG	greater than J	small wide grossly notched J	prominent N	M
	6. ME	tall wide greater than J	small wide J and prominent J''		M
	7. SP	tall notched equal to J	wide notched J	prominent N	M
	8. TK	tall greater than J	wide notched J		M
	9. GS	wide notched	small coarsely notched widened J, large J''	prominent N	M
	10. LG	wide notched	wide notched J	prominent N	M
	11. CD	wide	wide notched J	prominent N	M
	12. HS	tall	wide coarsely notched	prominent L and N	M
	13. EC	tall greater than J	small coarsely notched J	prominent N	M
	14. MG	tall wide equal to J	grossly notched J	slightly prominent L and N	M
	15. JS	tall greater than J	deep I, wide notched J		M
	16. LE	wide	wide notched J, slightly greater than H	wide tall N	M
	17. SH	tall equal to J	wide J	prominent N	M
	18. AC	tall equal to J	wide, grossly notched J	prominent N	M
	19. AH	tall notched greater than J	grossly notched wide J		M
	20. MK	tall	wide notched J	prominent L and N	M
	21. MF	tall notched	wide notched J	prominent L and N	M
	22. HK	tall greater than J	deep I, low wide J	prominent L and N	M
Group II	23. MM	small wide	widened, notched J taller than H	prominent N	
	24. AR	small notched widened	J is taller, notched and widened	prominent L and N	
	25. HS	notched, widened	taller grossly notched widened J	slightly prominent N	
	26. AR	small	taller notched widened J		
	27. DB	small notched and widened	taller widened notched J		
	28. CS	small	grossly notched and widened J	prominent N	
Group III	29. JN	small widened	tall J, widened J''		
	30. AS	small wide	tall J, widened J''	prominent N	

categories, group 1 having the most abnormalities. The outstanding pattern presented by group 1 is that of a tall, widened, sometimes coarsely notched H wave, equal to or greater than the J in amplitude, with a small I wave, a widened, coarse or grossly notched low amplitude

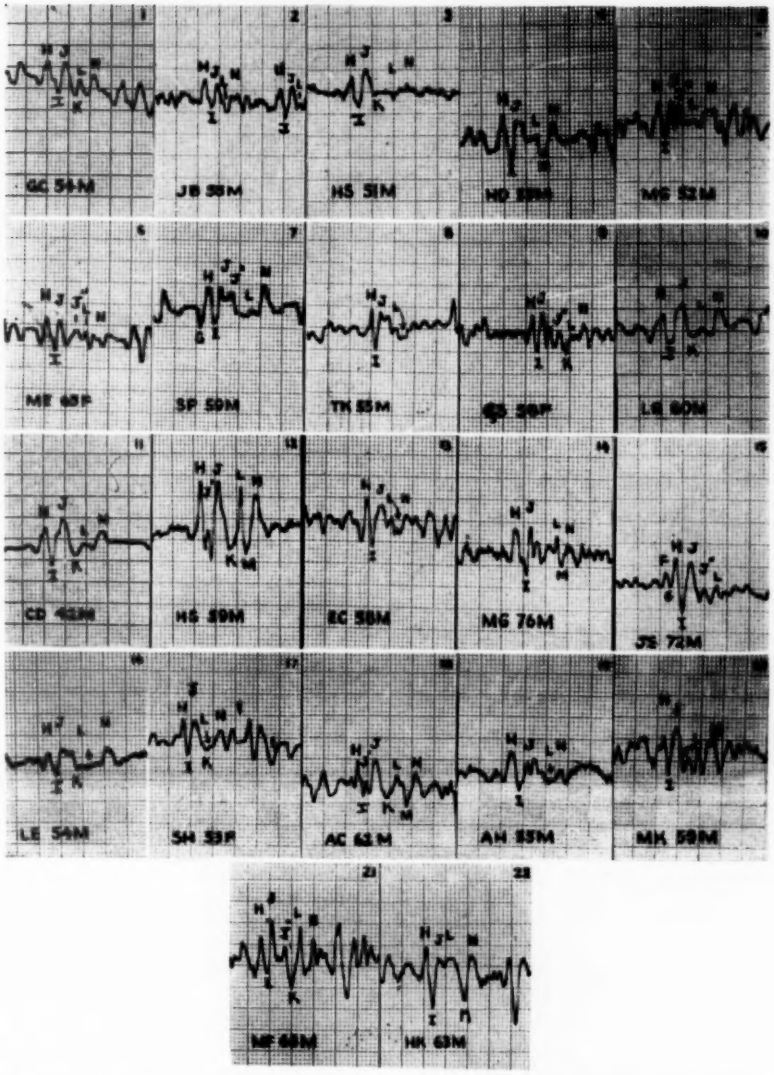

Fig. 6A. Group 1. The common pattern of the ultra-low frequency ballistocardiogram in 22 patients with myocardial infarction: A tall widened H wave equal to or greater than the J wave. Grossly notched J wave and frequently a tall N wave.

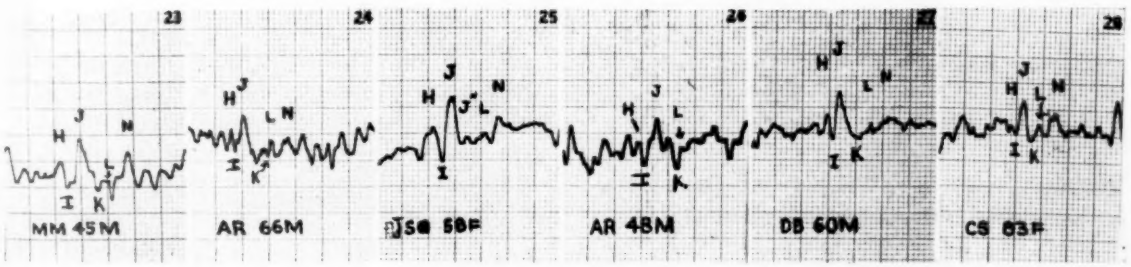

Fig. 6B. Group 2. Six patients with myocardial infarction who show the grossly notched tall J wave and frequent tall N wave.

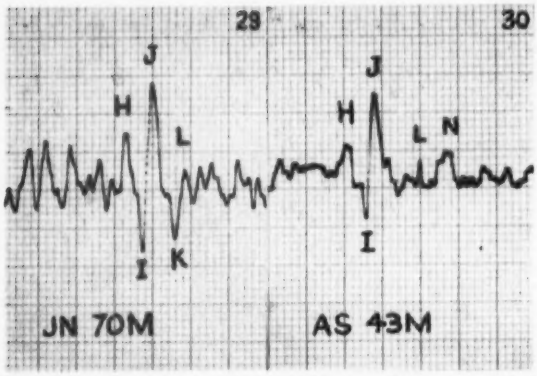

Fig. 6C. Group 3. Two patients with myocardial infarction who show a tall widened notched J wave and almost normal configuration.

J wave, and frequently a tall N wave. This pattern is present in all subjects in group 1, and has been termed the "M" pattern after that described by Starr.[2] Group 1 includes 22 of the 30 subjects or 73 per cent of the case material. The N wave was prominent in 14 tracings (46.5 per cent).

In group 2, there are six subjects, all presenting a wide, low amplitude, coarsely or grossly notched J wave. None of these six had a tall H wave equal to or greater than the J. For this reason, these six were placed in a separate group. The N wave was prominent in 4 or approximately 66 per cent of this group.

Group 3 contains the remaining two cases. The J complex is somewhat widened and notched, but is of greater amplitude, and has a less abnormal configuration. This type of J pattern has been seen in other post-myocardial infarct subjects in our series. The N wave was prominent in one of the subjects.

The tracings in Figure 8 were taken on a 50-year-old female during an attack of severe anginal pain, and two minutes after administration of nitroglycerin with complete relief. The anginal tracing presents a prominent F wave, a tall, slightly widened H wave larger than the J. The J-J'' is widened, L is small and the N is of greater amplitude than the J. The post-anginal tracing has reverted to a far less abnormal configuration with greater amplitude. The configuration during the period of anginal pain is very similar to those observed in post-myocardial infarction states, group 1 in our series.

The wide, abnormal J complex described

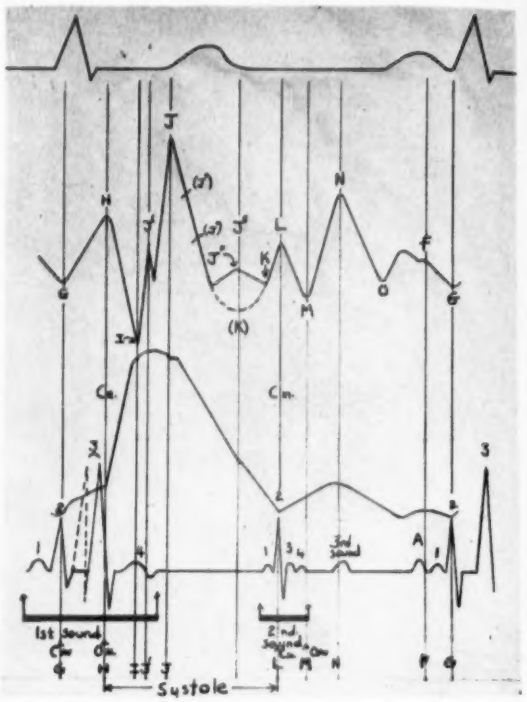

Fig. 7. An idealized, normal, ultra-low frequency acceleration (force) ballistocardiogram and the relations of its component waves to the electrocardiogram, the carotid pulse capsule tracing (air conduction) and to the low frequency apical phonocardiogram. Constructed from our normal tracings.

above was present in all subjects. The wide, tall H wave was present in 22 (73 per cent) of all the 30 subjects. It was wide in 27 of the 30 and tall in 23 of the 30. Thus, the wide H and J complex was diagnostic in over 90 per cent of the subjects. The N wave was very prominent in 20 of the 30 subjects or 66 per cent.

The pattern of group 1, a tall widened H wave equal to or greater than J, a widened grossly notched J wave, and a prominent N wave, is the pattern seen only in those patients who have sustained myocardial infarction. It has not been seen in the patient with a normal heart or heart disease of other types, including congential heart disease, left and right bundle branch block uncomplicated by infarction, and hypertrophy.

Discussion

The recording of the mechanical motions of the body associated with the cardiac cycle requires careful standardization of the apparatus

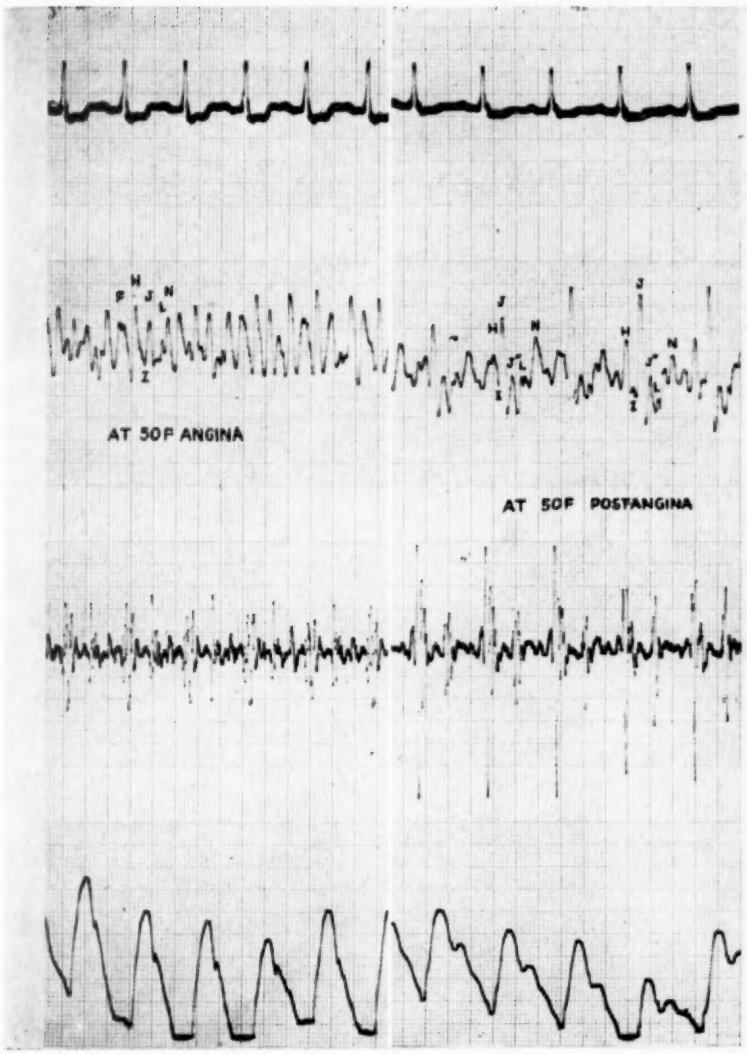

Fig. 8. Ultra-low frequency ballistocardiogram taken during an attack of angina pectoris and 2 min after the sublingual administration of gr 1/100 nitroglycerin, with relief of symptoms.

and the elimination of all artifacts and extraneous motions. The tracings obtained by the ultra-low frequency ballistocardiographic apparatus discussed herein are believed to be artifact free, and the references described in the introduction indicate that in the present state of our knowledge the ultra-low frequency technic of recording meets these requirements.

Tracings can be reduplicated in a single subject at any time in which the cardiovascular dynamics are not changing. Recordings made on different occasions and with different transducers on members of our own team have been of identical configuration with perhaps minor amplitude differences. In fact, these complexes are not unlike a signature and have been utilized as a method of testing our unit to determine its proper functioning.

Precise timing of the waves is necessary for accurate interpretation. The amplitude of the tracings records change in acceleration only, and by inference of mass times acceleration, the force. The timing, in comparison with the coexisting cardiovascular events, is almost identical

with that reported by Rappaport.[1] His terminology has been adopted by us (Fig. 7), but modified to meet the requirements of The Report of the Committee on Ballistocardiographic Terminology.[8]

The tracings of normal and diseased states presented have been selected from a large number of each type of disorder. A review of all our tracings has convinced us of two points: (1) The abnormal tracing is readily distinguished from the normal, and (2) certain ballistocardiographic patterns are evident and these are readily differentiated from each other. (Discussion of rheumatic valvular deformities will be submitted in a forthcoming paper.)

The description of the early "M" pattern of Starr[2] for post-myocardial infarction corresponds closely with the three tracings depicted in Figure 3. Each of these presents a tall, wide H wave followed by a low amplitude, widened and grossly notched J wave. The N wave is occasionally prominent and the H wave is often larger than the J. This description fits the tracings presented in group 1 (22 of our subjects).

Analysis of all 168 tracings has uncovered no "M" patterns in any other type of heart disease or clinically normal subjects. As far as our data indicate, this pattern appears to be specific for myocardial infarction. A few examples of "normal" hearts have been submitted to us for testing and were found to present this "M" pattern. Further delving into the past history and electrocardiograms of these subjects, and utilizing more detailed application of electrocardiographic exploratory chest leads and spatial vectorcardiography, have borne out the diagnosis of myocardial infarction.

Our small series of angina pectoris have given us the impression that these patients have in reality had previous myocardial infarctions. The ultra-low frequency ballistocardiograph changes observed are those we have seen only in myocardial infarction. The big difference between the ballistocardiogram of patients with angina pectoris and of those who have had a myocardial infarction that can be diagnosed by electrocardiogram and spatial vectorcardiogram, is that the former does not have a fixed pattern and can return after the attack to a less abnormal pattern than was shown during the attack. The ballistocardiogram of the myocardial infarction patient, contrariwise, shows a very marked decrease in amplitude and a tendency toward fixation of the abnormality.

The ballistocardiographic pattern of infarction appears to have no relation to the date of onset. We have numerous tracings taken on subjects many years post-infarction, and some as recent as a few weeks. These are identical in configuration, though not always in amplitude. We have followed occasional patients through the early and late stages following infarction with no apparent change in configuration. We can only speculate that the ballistocardiographic pattern of myocardial infarction represents a specific change in the functional powers of the heart. It seems obvious that the post-infarction heart now undergoes a series of contractions of a different character and of lowered forces.

To date, no Class 4 tracing of Brown,[3] i.e., tracing with unidentifiable waves, has been observed in our series. This system of grading the ballistocardiograph tracing in Classes 1 through 4 will probably require redefining in terms of the ultra-low frequency recording.

Variations of amplitude with respiration have been noted in the ultra-low frequency ballistocardiogram, similar to those seen in all other methods of recording. The respiratory phase, however, does not interfere with the recording of the ultra-low frequency acceleration ballistocardiogram, and it is not necessary to stop respiration to obtain the record. However, part of our routine has been the taking of records in quiet suspended expiration and inspiration as well as during normal quiet breathing. In all patients in the myocardial infarction series, no particular change or improvement of amplitude followed inspiration. This finding would suggest that the myocardium is unable to improve the force and quality of ejection as normally occurs during the respiratory cycle. This observation may be related to the amount of myocardial reserve. Why a single pattern of forces will develop regardless of location of damaged muscle cannot be explained at this time.

Regarding the other findings of Starr[2]

obtained with his high frequency bed, we have seen no patterns which would coincide with the "late M" pattern. We have observed prominent L waves in seven of the group 1 series, one of the group 2, and none of the group 3.

The findings of excessive notching in the J and K waves of the acceleration tracings described by Smith and Rosenbaum[6] are evident in our series. Part of the pattern of infarction appears to be gross notching in the H and J and probably all waves.

Conclusions

(1) The normal cardiovascular system presents a specific characteristic, ultra-low frequency ballistocardiographic appearance, readily recognized and differentiated from the abnormal.

(2) Component ballistocardiographic waves are related to specific events in the cardiac cycle, best determined by timing with a simultaneous phonocardiogram and carotid pulse tracing.

(3) A characteristic, apparently specific abnormal pattern (the "M" pattern of Starr) has been found in the majority of subjects who have sustained myocardial infarction:

(a) This pattern has not been found in other types of cardiac disease or in normals.

(b) It remains apparently unchanged for years after recovery.

(c) A number of "silent" infarcts have been uncovered with this method.

Acknowledgments

Mrs. Rita Shulman has rendered invaluable technical assistance. The spatial vectorcardiograms were interpreted by Stephen R. Elek, M.D.

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Coronary Artery Disease—Present Concepts*

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IT WOULD seem that the incidence of coronary artery disease has sharply increased; however, much discussion has concerned itself with whether this increased incidence is real. Edward A. Lew of the Metropolitan Life Insurance Company at a recent conference on atherosclerosis and coronary heart disease presented data to prove that the increased incidence was in fact quite small. His primary argument concerned the fact that we were now dealing primarily with an older population in whom a higher incidence of coronary artery disease would naturally be expected. His data further indicated that coronary artery disease had become a "popular" diagnosis, but he also suggested that some of the apparent increased incidence was due to better diagnostic ability. The important fact is that the incidence of the disease is currently very high and this indeed represents a major national health problem.

It might be well to define at this point what is meant by coronary artery disease. Here we include all the diseases of the coronary arteries due to atherosclerosis no matter what the syndrome may be. That is to say, it includes coronary insufficiency, transient and manifested clinically by angina pectoris, coronary insufficiency (acute, protracted or chronic) and acute coronary occlusion with or without myocardial infarction. Fortunately, coronary artery disease due to atherosclerosis is now being treated as a true "disease process" rather than an inevitable consequence of the aging process. Now that it is considered a disease, the etiologic factor is being sought in the attempt to control and reduce its incidence. On the other hand, accepting the fact that our major problem currently is discovering the etiology, we must also attempt to help those who are already afflicted with the disease in its various clinical entities today.

Advances in Diagnosis: What do we know about the diagnosis of coronary artery disease that represents an advance over what could be accomplished in diagnosis some years ago? When one reviews James Herrick's original article written in 1912 on "Clinical Features of Sudden Obstruction of the Coronary Arteries",[1] it must be concluded that little has been added to the diagnosis of this disease on the basis of case history and physical examination. Perhaps in better understanding pain equivalents, particularly the symptom formerly classified as "acute indigestion", we have added to our diagnostic acumen. Also, we are now able to diagnose with a greater degree of accuracy the complications of an acute myocardial infarction, for example, the rupture of a papillary muscle, the perforation of a softened septum, actual rupture of the heart, and the post-infarction form of pericarditis as described recently by Dressler.[2] From the laboratory standpoint, however, much has been added such as the use of the C-reactive protein test, transaminase determinations, multiple-lead unipolar electrocardiography, the Master 2-step exercise test for coronary insufficiency, and vectorcardiography. Professor Malmros of Lund, Sweden has even devised ultrasonic radar-type equipment for detecting the size and location of a recent myocardial infarction.

ETIOLOGY OF CORONARY DISEASE

In discovering the cause of coronary artery disease many factors must be considered. Let us first examine the factor of age. No longer is this disease considered one afflicting only the

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aged. There is autopsy evidence to prove that even infants have died due to disease of the coronary arteries, and we are constantly seeing younger patients, particularly men in their late twenties and early thirties, stricken with the disease. Heredity must be considered an important factor in the development of disease of the coronary arteries. It would appear that the kind of arteries we inherit might make us particularly vulnerable to later atherosclerotic invasion of the blood vessels. Indeed, if this be true, much of our present investigation would need reconsideration, and genetics would have to assume a more dominant role.

The factor of sex must be important in atherogenesis. All the available data indicates that coronary artery disease is common in males before the age of forty whereas menstruating women are relatively immune. Naturally this invokes a hormonal etiology in atherosclerotic disease of the coronary arteries.[3]

The attempt to correlate our present "stressful" existence with the increased incidence of coronary artery disease is a difficult concept to prove. It is claimed that this is primarily a disease of civilization. That is to say, our present-day mode of living, with its competitive drives, particularly as practiced in the United States and countries with comparable high industrialization and high living standards, might in some way alter the metabolism of the blood vessels. This theory assumes that the less civilized people such as the indigent African Negro, who certainly live in insecurity and stress, are not affected by these factors. Certainly there is little data to support the stress factor in atherosclerosis.

The concept of somatotypes has recently gained some recognition as related to disease entities. In so far as coronary artery disease is concerned it is claimed that the mesomorphic individual (broad, muscular build) is particularly vulnerable. Insurance actuary data would indicate that obesity as it alters somatotypes is most important in this respect.

Cholesterol and Lipoproteins: Another factor is that of the chemotype, or more specifically an analysis of some of the chemical constituents of the blood of the individuals who are likely to develop disease of the coronary arteries. In my own experience the young male afflicted with the disease usually has an elevated blood uric acid. Gertler and White long ago claimed that the CUP index (Cholesterol-Uric Acid-Phospholipid Index) was of greater diagnostic significance than any of these factors considered individually.[4] High blood levels of Svedberg flotation unit as a measure of blood lipids have been incriminated as etiologic agents in the pathogenesis of this disease by a group of investigators headed by Gofman.[5] In spite of repeated attempts to relate S_f 12–20 and 20–200 units to atherogenesis much of the data presented is conflicting. A recent report would seem to indicate that as a predictive test of coronary artery disease, determination of lipoprotein fractions falls short of its mark and in many respects is not as accurate as the simple determination of blood cholesterol values. The solubility of cholesterol seems to be maintained by plasmatic stabilizers, for example, heparin, fatty acids and phospholipids. When these are lowered, the solubility of the cholesterol-lipid-lipoprotein is altered and plaques of cholesterol deposit themselves in the coronary arteries. In the electrophoretic study of the plasma lipids, a consistent elevation of the beta lipoproteins in individuals with atherosclerotic disease of the coronary arteries has been demonstrated. Perhaps the most publicized atherogenic factors have been cholesterol and fat-rich foods.

Now let us examine the facts of why cholesterol and fat foods should be important in the production of this disease. First of all, cholesterol is invariably present, thereby being a major component of atherosclerotic plaques. In addition, the average serum cholesterol is higher in patients with manifest coronary atherosclerosis. Furthermore, it is an established fact that there is premature atherosclerosis in patients with high blood cholesterol levels such as occur in diabetes mellitus, nephrosis, hypothyroidism and familial xanthomatosis. In the laboratory, atherosclerosis can be produced experimentally by feeding high cholesterol diets, and recently, labeled cholesterol included in the diet of a patient who was dying, appeared in the atherosclerotic plaques as seen at autopsy. However, many people eat large quantities of fatty foods and food with a high-cholesterol content and

never do get atherosclerosis. In certain respects this can be compared to the metabolism of carbohydrates in normal individuals contrasted to the abnormal metabolism of carbohydrates as occurs in diabetes mellitus. The average American diet consists of 40 per cent fat and contains 500 mg of cholesterol, but the body synthesizes many times this amount from acetate, pyruvate, and other products of fat, protein and carbohydrate metabolism. Therefore, many investigators claim that exogenous cholesterol has little or no effect on the blood level of cholesterol.

Treatment

Diet: Let us examine some of the methods that have been used to decrease the lipid-lipoprotein-cholesterol factors in the blood. The elimination of certain foods from an individual's diet, particularly fats in their saturated form, has been advocated. Ancel Keys is particularly impressed that this is an important preventive measure. Other investigators have even suggested that the government go on record with recommendations that the fat content of our diet be reduced, and the armed services have given serious consideration to such a suggestion. When last reported officially no such recommendations were contemplated. Recently the American Medical Association's Council on Food and Nutrition rendered this opinion: "Quite a bit more study concerning dietary fats will have to be done before the average American eating habits are to be drastically altered."[6] However, it would seem fair to recommend low-fat and low-cholesterol diets if an individual has a family history of early death from coronary artery disease and also has a high level of blood cholesterol.

Other Measures to Reduce Blood Cholesterol: Lipotropic agents such as choline, lecithin, and inositol have been used for many years. At best the results with these products are equivocal. *Anticoagulants* such as heparin, dicumarol and related compounds are used in the treatment of an acute myocardial infarction. In more recent years it has been claimed by a group of investigators that if these agents are used early enough they may prevent coronary thrombosis when coronary occlusion is impending. This concept remains to be proved.

Thyroid and *thyroid analogues* are able to decrease the level of blood cholesterol. This concept naturally arises from the fact that the blood cholesterol is low in hyperthyroidism and high in hypothyroidism. A Mayo group of investigators recently reported that *nicotinic acid* has been found to be valuable in lowering the level of blood cholesterol.[7]

Sitosterol has been introduced as an efficient method to reduce the blood cholesterol value. The rationale is that it represents a chemical analogue of cholesterol, and as such theoretically blocks the absorption of cholesterol by competing for enzyme mechanisms. In the gastrointestinal tract sitosterol combines with cholesterol to form a "one to one" mixed crystal that is relatively insoluble, and therefore is not available for absorption. Because of the enterohepatic circulation of cholesterol, any substances that block intestinal absorption will also block the reabsorption of endogenous cholesterol secreted into the bowel as well as the dietary cholesterol. Fat foods stimulate the liver to produce cholesterol—how and why is not known.

However, this does not occur with fats composed predominantly of unsaturated fatty acids. The blood cholesterol level usually decreases with the use of corn oil and sun-flower seed oil, and even with certain fish oils which are highly unsaturated. However, unsaturation is not the only factor.[13] A rise in cholesterol has been observed occasionally even after the consumption of such unsaturated fatty acids. At present Keys recommends a low-fat diet and when necessary this is supplemented with corn oil. Recently an emulsion of safflower oil, a highly concentrated source of unsaturated fatty acids, has been marketed as an aid in the management of atherosclerosis.

Estrogens have been used on the basis of the fact that they will reduce the level of the beta lipoproteins. Barr demonstrated that of the lipoproteins, the beta fraction was usually increased in the presence of atherosclerotic disease of the coronary arteries.[8] He also found this to be true in young women who were oophorectomized for medical reasons. On the basis of this information a detailed study was begun on such women. Katz and his colleagues at the Michael Reese Hospital in Chicago also are engaged in a long-term study using estrogens on

young men who have had one attack of coronary occlusion with myocardial infarction. As of today it would seem that estrogens might offer some protective value to such individuals, but it is still too early for final evaluation.

Immediate Treatment of Acute Myocardial Infarction: At this point it would be well to relate some of our present thoughts on the immediate treatment of patients who have sustained an acute myocardial infarction. I will not discuss in any detail the emergency treatment of the shock-like state precipitated by such an attack in which the use of morphine derivatives is mandatory. Rather, I would like to discuss the more controversial topics such as the use of *anticoagulant therapy* and the *armchair treatment.* At the present time a battle is waging between the group contending that every patient who sustains an acute myocardial infarction should have anticoagulation and the group in favor of withholding such therapy in "good risk" patients. Wright[9] is the protagonist and has rendered his report under the auspices of the American Heart Association, and Russek[10] is the antagonist in this debate. The basic problem is this: Russek feels that he can recognize "good risk" patients and claims that in such patients the use of anticoagulation is undesirable, because it adds the risk of bleeding phenomenon, the expense of medication, and the frequent use of venopuncture to control adequately the prothrombin levels. On the other hand, Wright insists that it is impossible always to correctly identify such a "good risk" patient and frequently cites, and I agree, that a patient who has apparently started as a "good risk" patient may suddenly become a complicated case or even die. For this reason he claims that most patients who sustain an acute myocardial infarction, and in whom the anticoagulants are not contraindicated, should receive the benefit of these drugs.

During the war when it was necessary to return men to duty promptly, early ambulation was established as a desirable feature of convalescence from any major illness. Samuel A. Levine of Boston modified this concept when he applied the therapy of "armchair treatment" to patients who had sustained an acute myocardial infarction. Let me emphasize at this point that armchair treatment is not early ambulation, but merely a change in the patient's position from the recumbent to the sitting. It is claimed by those who use this therapy that the patient's morale is improved, the incidence of thrombophlebitis is lowered, and congestive failure when present is more comfortably managed. As used by Levine, the patient is placed in his armchair at the side of the bed shortly after the acute coronary occlusion has occurred. Many of us have modified this program so that our patients, while not being placed in the armchair at this early date, are permitted to be out of bed after about a week.

Another notable advance in the therapy of the acute attack of myocardial infarction includes the use of *procaine amide* when ventricular premature beats occur frequently or in a paroxysm. The use of *pressor amines* in the management of shock secondary to acute myocardial infarction is now well established. Probably the most widely used of these drugs is Levophed (levarterenol bitartrate) in the intravenous form. A 4 cc ampule of this 0.2 per cent solution is diluted in 1,000 cc of 5 per cent glucose in water or saline. After observing the response to an initial dose of 2 to 3 cc/min, the rate of flow is adjusted to establish and maintain an optimum blood pressure. Recently there has been a report of the use of *pump oxygenators* to complement the work of the heart in the acute phase of the myocardial infarction; the theory is that the work of the heart is reduced when an artificial mechanism for oxygenating the blood is added to the circulation. This report is much too new to warrant any further comment.

In the management of the patient who has coronary artery disease it has become common practice to permit a greater participation in *activity* than was thought wise before. The outstanding example of this "new outlook" has been expressed in the management of our President. It is claimed by many capable clinicians with long-term experience as exemplified by Paul D. White that the increased activity is actually good for the development of collateral circulation. Certainly one feature has manifested itself very dominantly. We no longer feel that these patients should be invalided, and in many cases they may even return

to a job that requires considerable physical effort.

Induced Hypothyroidism: Now let us go on to other methods for the current management of patients with coronary artery disease. The work of Herman Blumgart has extended over a long period of time and is well known. The rationale of Blumgart's contribution to the management of intractable angina pectoris and congestive heart failure involves lowering the metabolic rate of the patient and thus secondarily, the work of the heart.[11] In the beginning this was accomplished by producing hypothyroidism, either surgically or by the use of anti-thyroid drugs, but today this is accomplished through the use of radioactive iodine. His results are encouraging, but the method is not physiologic and involves the substitution of one disease for another. However, the symptoms of hypothyroidism are usually controlled by the administration of thyroid extract, and Blumgart and his associates feel that the hypercholesterolemia produced by the hypothyroid state is not atherogenic.

Surgical Measures: Attempts to revascularize the heart have been spearheaded through the efforts of Claude Beck. The Beck I and II procedures have been widely publicized, and Beck's work is monumental in this respect. Dwight Harken of Boston has used de-epicardialization, the application of phenol, and the attempt to revascularize the myocardium by the application of the lingula of the lung. Charles Bailey of Philadelphia has even attempted the direct approach by actually reaming out the coronary arteries involved in atherosclerosis. As this paper is being written, the work of Robert Glover seems to hold the spotlight. This involves the ligation of both internal mammary arteries. Glover claims no originality for the procedure and states that it is still too early to evaluate properly his results. The rationale of the procedure involves increased blood flow to the visceral pericardium (and hence the myocardium) by way of the pleuropericardial arteries. At a recent meeting in Washington, D. C., James Kitchell, his medical colleague, reported encouraging results in about 70 per cent of the patients (fifty in number) in whom the procedure was accomplished.[12]

Resuscitation Measures: A few months ago a report appeared in the Journal of the American Medical Association stating that a doctor while on his hospital rounds had actually died of an acute myocardial infarction. However, by rapid thoracotomy and cardiac massage, circulation was re-established, and the patient was able to return "from death" to his work shortly thereafter. Dr. Edgar F. Berman and his associates in Baltimore recently described a dramatic heart replacement operation in animals. Proper evaluation of these reports bears further consideration. It is conceivable that in the future a patient afflicted with disease of the coronary arteries might be supplied with an extracardiac source of energy that will assume the mechanical function of the heart while it is being serviced. Perhaps the most dramatic of any present measures in the management of disease of the heart is the actual substitution of an artificial heart. Attempts in this direction are now in progress, and it is not inconceivable that a working model will soon be available.

As in every other disease much of what is written here today will be obsolete in a short period of time, but one thing seems sure. Coronary artery disease will be conquered, and it is most likely to be accomplished by discovering its etiologic factors. When this is found, prevention should soon follow.

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The Surgical Therapy of Occlusive Coronary Artery Disease—Present Status*

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THE POOR prognosis of occlusive coronary artery disease has been emphasized by Parker and his associates,[1] who reported a series of more than 3,000 cases with angina pectoris, none of whom survived after five years. Katz and his co-workers[2] have reported that 25 per cent of their patients who suffered a myocardial infarction were dead in two months, 50 per cent in one year, and 75 per cent in three years. Obviously, in light of the gravity of the disease, intensive efforts to develop a technic for the revascularization of the ischemic heart seemed warranted.

In order to properly evaluate the various surgical procedures proposed for the treatment of coronary artery disease, the basic pathologic physiology of the disease and the objectives of attempted surgical therapy must be understood.

At the outset it must be conceded that the surgical approach to the therapy of coronary artery disease can be only palliative. The surgeon as yet has been unable to completely remove the atherosclerotic placques or prevent their recurrence; nor can operative procedures *per se* be expected to prevent future coronary occlusions.

The surgical therapy of coronary artery disease is designed to accomplish two things: first, the amelioration of the symptoms of angina pectoris; and second, protection against ventricular fibrillation in the event of a future coronary occlusion, by the introduction of relatively small quantities of blood to the ischemic myocardium through extracoronary collateral circulation.

In this connection, the reported experiments of Hellerstein and Beck[3] are of interest. They found that should the left anterior descending coronary artery be suddenly ligated at its origin, experimentally, there is a 66 per cent mortality. However, should all of the small vessels supplying a small area, 1 cm in diameter, on the antero-lateral aspect of the left ventricle be ligated, there is a 100 per cent mortality, due to ventricular fibrillation. This experiment emphasizes two points. First, rendering a relatively minute area of myocardium ischemic may initiate a trigger mechanism which trips the heart into ventricular fibrillation. Obviously, there would have been adequate myocardium to continue life had fibrillation not been induced. This phenomenon they termed "mechanism death." Again, if a single small vessel remains unligated, ventricular fibrillation does not ensue. This demonstrates that a small quantity of blood to an ischemic area may prevent the production of this trigger mechanism, and thereby protect the heart against ventricular fibrillation.

Schlesinger,[4] and Prinzmetal, *et al.*,[5] have demonstrated that the myocardial ischemia caused by coronary atherosclerosis stimulates the development of *intra*-myocardial collateral circulation. It is therefore of no interest to the cardiologist should a procedure be demonstrated to open these collaterals. The procedure of choice is obviously that which is capable of effecting an ample *extra*-coronary collateral circulation.

It might be well at this point to briefly discuss the procedure of arterialization of the coronary sinus from the point of view of historical

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interest. The operation, described by Beck, *et al.*,[6] consisted of a two-stage procedure. At a first stage, a vein graft was placed between the descending aorta and the coronary sinus, thus producing an arterio venous fistula. At a subsequent second stage, the coronary sinus proximal to the venous graft was ligated over a probe to 2 mm in diameter, thus attempting to retroperfuse the myocardium through the "back door" so to speak. The concept of nourishing an organ by utilizing its venous tree as a portal of entry to the capillary bed was quite ingenious, and, in fact, some initial benefit was demonstrated by Eckstein and associates,[7] and Bakst, *et al.*[8] However, these investigators demonstrated that after three to six months the procedure ceased to protect the heart against coronary occlusion. Pathologic section of the specimens revealed a complete obliteration of the venous tributary bed to the coronary sinus by a severe degree of intimal proliferation. Apparently, this was initiated by the arterial pressure within a venous bed not built to tolerate it. The procedure was therefore self-limiting.

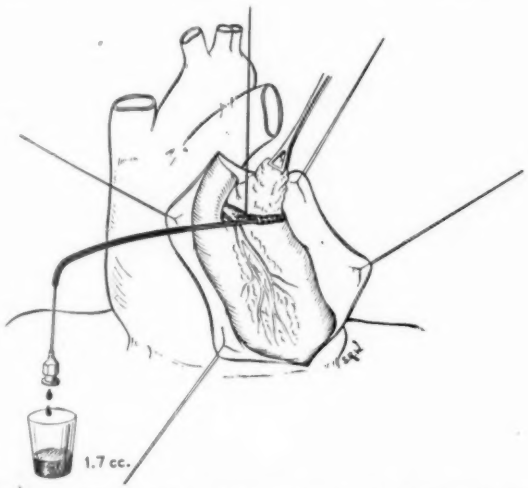

Fig. 1. When the peripheral segment of the ligated circumflex coronary artery is cannulated, a continuous flow of arterialized blood is obtained. This flow is a measure of inter-coronary collateral circulation.

Methods

It has been our aim to evaluate the various procedures designed to augment the coronary circulation via its collaterals. Towards this end, we have used two physiologic tests.

In the control animal, when the circumflex coronary artery is ligated at its origin and the peripheral segment of this vessel is cannulated, a steady retrograde flow of arterial blood emerges. This blood must have arisen from neighboring arteries, and is a measure of the normal inter-coronary collateral circulation. This normal figure averages 1.7 cc per minute. The peripheral pressure in this vessel averages 30 cm of water. These backflow studies seem to be a fairly reliable index of changes within the coronary arterial circulation (Fig. 1).

Next, perfusion experiments were performed with the heart *in situ*, as follows: Ventricular fibrillation was induced after the animal was heparinized. The ascending aorta was doubly clamped above the origin of the coronary arteries. The descending aorta was cannulated at the diaphragm, and the arch and descending aorta were perfused with a red neoprene latex solution at a pressure of 160 to 180 mm of mercury. In this manner, since none of the perfusate could reach the coronary arteries through their normal ostia, any perfusate found within them must have entered through the collateral circulation (Fig. 2).

These physiologic tests were then applied for assessing the various procedures designed for the surgical correction of coronary artery disease by augmenting the extra-coronary arterial collateral circulation.

Results

Pericardial Poudrage: A group of animals, prepared with pericardial poudrage as described by Thompson,[9] were examined after 6 to 8 months. The retrograde blood flow from the peripheral segment of the ligated circumflex coronary artery averaged 5.5 cc/min, which was a threefold increase over the expected normal value. The peripheral pressure was normal. The perfusion studies demonstrated the ability of pericardial poudrage to initiate the development of *extra*-coronary arterial collateral circulation. With this technic, 50 per cent of the animals demonstrated complete filling of the circumflex coronary arterial tree. Since the perfusate could not enter the coronary arteries through their normal ostia, the filling of the circumflex coronary arterial tree was strong evidence of the

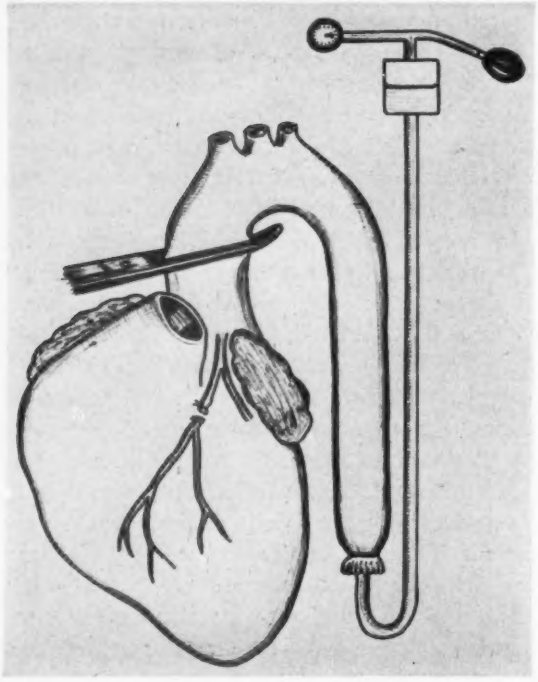

Fig. 2. With the heart *in situ*, the ascending aorta is clamped distal to the orifices of the coronary arteries. The descending aorta is cannulated, and the arch and descending aorta are perfused with a neoprene latex solution at a pressure of 160–180 mm Hg.

Under these conditions, any material found within the coronary arteries could not have entered through their normal ostia, and must have arisen from extracoronary circulation.

presence of *extra*-coronary arterial collateral circulation. It should be stated that the coronary arterial tree could not be filled with this technic in a control series of animals. Thus, pericardial poudrage effectively produced extracoronary arterial collateral circulation with the circumflex coronary artery.

De-epicardialization: The second procedure evaluated with these technics was the modification of pericardial poudrage described by Harken *et al.*[10] These investigators suggested that the epicardium presented a barrier to the ingrowth of new blood vessels to the myocardium by pericardial poudrage, and, therefore, that it had to be destroyed. They suggested that this could best be done chemically, using 95 per cent phenol.

In this group, the retrograde circumflex coronary artery flow averaged 3.8 cc/min, with a normal peripheral pressure. The perfusion experiments, however, demonstrated that the procedure was ineffective. In 11 animals, there was no filling of the coronary arterial tree, with scant filling in a twelfth. This in no way compared to the filling demonstrated in the simple poudrage group. It would seem that the addition of phenolization of the epicardial surface to the technic obviated the beneficial effect of the procedure. This was subsequently borne out clinically. In two patients in whom the combination of phenolization and poudrage was performed (prior to the securing of the experimental results), though there was an initial amelioration of symptoms, the severity of the angina has returned.

Implantation of Internal Mammary Artery: The procedure of implantation of the internal mammary artery into the left ventricular myocardium as described by Vineberg[11] was next evaluated. The operation entailed the dissection of the internal mammary artery from the anterior thoracic cage between the third and seventh intercostal spaces. All intercostal vessels were ligated, two or three of the larger ones being prepared for future implantation. The site for the intramyocardial tunnel was selected so that the implanted vessel was not kinked. The preserved intercostal vessels were transected so that they bled actively, before the internal mammary artery was pulled into the tunnel. Despite the active bleeding of the implanted intercostal vessels, intramyocardial hematomas did not develop. Vineberg explained this phenomenon by suggesting that the blood was drained by the Thebesian system. In a previously reported group of animals in which the internal mammary artery was implanted into the ventricular myocardium, very little benefit to the heart could be demonstrated.[12] Pathologically, the lumina of the implanted vessels were almost completely obliterated by intimal proliferation. These results were discussed with Dr. Vineberg who suggested that the occlusion of the implanted vessel by intimal proliferation might have been due to a lack of need for this blood by the normal heart. He suggested that the experiment be repeated in a group of animals in which myocardial ischemia was created to stimulate a need for the introduction of a collateral circulation. Consequently, in this group, myocardial ischemia

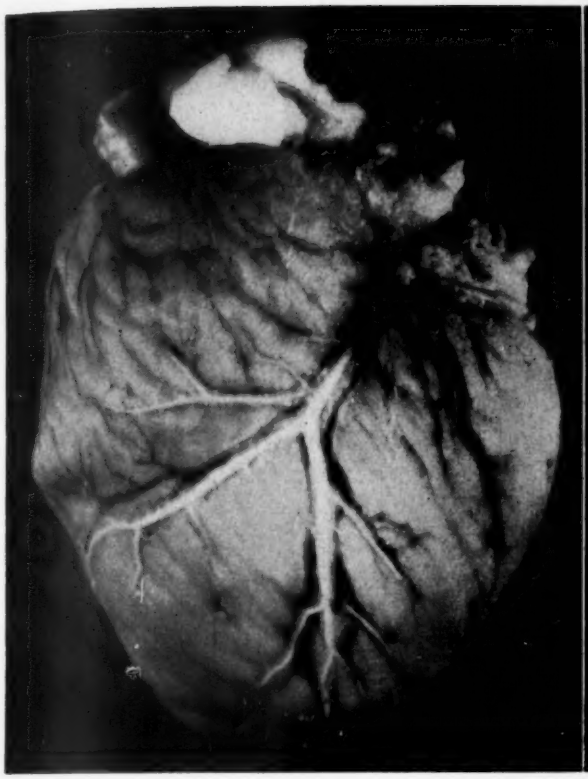

Fig. 3. Vineberg heart, perfused according to technic described in Figure 2. Note that both the anterior descending, and circumflex arteries are completely filled with the perfusate.

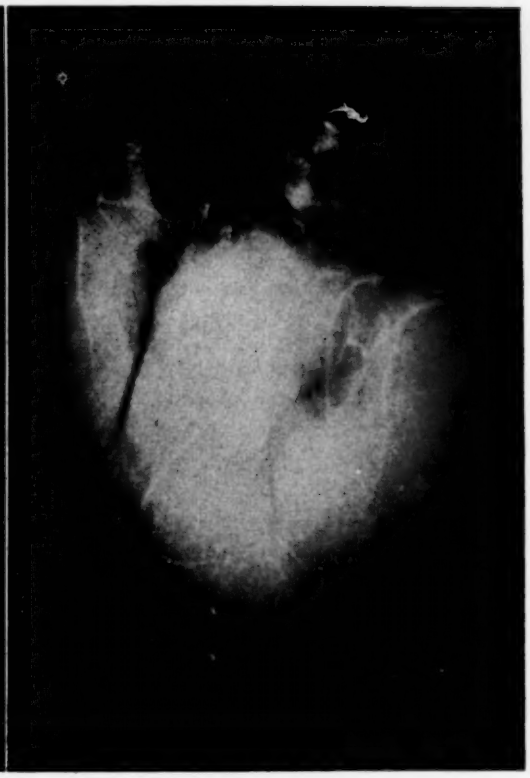

Fig. 4 X-ray of specimen in Figure 3. Note the complete filling of the many small intramyocardial vessels.

was produced concomitant with the implantation of the internal mammary artery, by partially ligating the anterior descending coronary artery to 2 mm over a probe, using a specially prepared reactive polyethylene material. It was hoped that this material,* which contained a high concentration of dicetyl phosphate, would stimulate fibroblastic proliferation, and thereby gradually complete the occlusion of the vessel. Moreover, the initial partial occlusion of the vessel was not considered adequate unless the anterior aspect of the left ventricle became slightly cyanotic.

In this series, the results were most impressive. To begin with, the retrograde blood flow from the peripheral segment of the anterior descending vessel averaged 12 cc/min, and the peripheral pressure in this vessel averaged 90 cm of water. Occluding the implanted internal mammary vessel proximal to the intramyocardial tunnel, was followed by an immediate fall in pressure and flow to normal limits. When the clamp was reopened, there was a rise of pressure and flow to the previous high values. This seemed to indicate the presence of collateral anastomoses between the implanted internal mammary artery and the peripheral segment of the ligated anterior descending coronary artery.

The results of the perfusion studies were even more striking. Again, it must be recalled that since the perfusate could not enter the coronary arterial tree through the coronary ostia, any filling of these vessels must have taken place through extra-coronary anastomoses. There was good filling of the anterior descending artery and its branches in 90 per cent of the animals. In addition, there was good filling of the circumflex coronary artery in 25 per cent, and of the right coronary arterial tree as well, in 10 per cent. Roentgenographic examination of the specimens revealed even more complete filling of the

* Prepared by duPont de Nemours & Co., Inc., and is called duPont Polyethylene Film, Type NV-7-14.

vessels than could be realized by gross examination (Fig. 3 and 4).

The results of internal mammary implantation into the left ventricular myocardium seem to be most convincing. It seems that though the procedure is ineffective when the myocardium is not ischemic, there is a remarkable production of *extra*-coronary arterial anastomoses when it is.

Discussion

From these experiments, a definite opinion has developed as to the procedure of choice for the surgical therapy of coronary artery disease. Poudrage seems to effectively fill the circumflex coronary artery in 50 per cent of the animals. Internal mammary implantation demonstrates good filling of the anterior descending artery in 90 per cent of the specimens, and of the circumflex coronary arterial tree in 25 per cent. It therefore seems that each of these procedures is effective in producing *extra*-coronary collateral circulation to a segment of the coronary arterial tree. Our present concept has matured to a combination of these procedures to protect both the anterior and postero-lateral portions of the left ventricle against coronary artery occlusion. This consists of the implantation of the internal mammary artery into the anterior wall of the left ventricle, combined with the instillation of magnesium silicate posteriorly and posterolaterally over the wall of the left ventricle.

The Vineberg technic has been modified in that it is performed through an anterior approach which not only facilitates the dissection of the vessel, but also permits the patient to be placed in the supine position. The latter has been repeatedly demonstrated to be that best tolerated by the cardiac patient.

Conclusion

In conclusion, it seems to have been demonstrated that pericardial poudrage as described by Thompson is effective in producing *extra*-coronary collateral circulation to the circumflex coronary artery. Implantation of the internal mammary artery, on the other hand, effectively produces extra-coronary arterial collateral circulation with the anterior descending artery. It is natural to evolve upon a combined procedure for the protection of the left ventricular myocardium against occlusion of both major vessels.

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Symposium on the Cardiac in Industry*

Introduction

C. Richard Walmer, M.D.†

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There can be little doubt of the interest of industry and the industrial physician in the whole subject of cardiovascular disease. The fact that this entire session of the meeting of the American College of Cardiology is devoted to the industrial aspects of heart disease is in itself sufficient proof of this interest.

About five years ago, Dr. Edward M. Kline of Cleveland, speaking on this podium, estimated that about 400,000 persons with coronary disease were being added yearly for the period of their survival to the labor market. He pointed out that, because of the constant increase of the number of aging persons, the number of cardiac patients in industry can be anticipated to increase even further.[1] Since then, several authorities have reported their experiences in dealing with employees having some type of cardiovascular diseases. Very recently, Thompson and Huntington reported on 430 employees of the Phillips Petroleum Company with definite cardiovascular disease.[2] These cases were discovered in the course of 13,000 voluntary periodic health examinations made in two years, and were studied on the basis of placement and performance. The study indicated that the recognized cardiac can and does work productively with the proper job placement. It was the undiagnosed cardiac that posed the problem and the threat. Kline, in the paper referred to heretofore,[1] has given a complete and detailed discussion on the method by which the problem of placement and evaluation has been successfully approached by the Work Classification Clinic of the Cleveland Heart Society. A number of other such clinics have been established since that time, including one here in Pittsburgh.

It is necessary for the proper placement of employees with some history or symptoms of cardiac disease that the industrial physician have a complete and thorough knowledge of the demands of the various jobs. This is also essential in determining when a cardiac patient should return to work, as such a decision cannot be made merely on the basis of his physical condition. Successful rehabilitation and placement require a complete and thorough knowledge of the demands of the job to which that patient is returning. Such knowledge includes not only the physical demands of the job, but the characteristics of the environment, the attitude of the co-workers and superiors, and the attitude with which the patient approaches his job. Many jobs demand less physical exertion than one might think from the titles they bear.

I think one finds it usually the case in the larger companies or those with full time medical departments that the plant physician has detailed knowledge of the individual processes and operations and their hazards and particularly, the demands and requirements of each job. In far too many instances, however, the examining physician, and certainly the patient's

* Presented at the Fifth Interim Meeting of the American College of Cardiology held at Mellon Institute, Pittsburgh, November 28, 29 and 30, 1956

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personal physician, have only the vaguest idea of the demands and requirements of the job. Consequently, patients are sometimes returned to positions beyond their capabilities and sometimes denied the opportunity to return to work which they could easily handle. Dr. Thorpe will have more to say along these lines in his discussion of the problem of continuing the employment of individuals partially disabled by heart disease.

Proper placement of the individual in industry has been aided by the use of the electrocardiograph, which in turn has provided records which are most useful in determining the effectiveness of such a program. Dr. McGee's work in 1953[3] was a significant contribution to the evaluation of the use of the electrocardiogram in industrial medicine. He and his co-workers had an opportunity to study approximately 37,000 tracings on over 7,000 individuals. One conclusion was that myocardial infarction is not frequently recognized. Another important finding in this study was that the worker's productive capacity was not indicated by the tracing alone, and that the best use of the worker's capacities depended upon the physician, the employer, organized labor, and the administrators of the compensation laws.

I believe that Dr. Price in his discussion of the occurrence of heart disease among industrial workers will have more to say about the study of data based on electrocardiographic findings.

Certainly much more information is needed to combat effectively heart disease both in the general public and in the industrial population. The many programs of various branches of the Public Health Service can be expected to give us some of this badly needed knowledge. Dr. Chapman will give a summary of these activities. The nursing services and work classification units which are functioning as a part of the Public Health Service's Heart Disease Control Program, will, I am sure, contribute greatly to the solution of the problem.

The subject of rehabilitation of the cardiac will be dealt with in greater detail by Doctors Kahn, Bennett, and Klein. They, too, will enlarge on the functions of the physician, industry, and government in this important problem.

The relationship between work and the development of heart disease can be determined only by further research. Experimental work in this area points out the wide gap between animal toxicity studies and their proper interpretation in relation to effects on man. In our own work at Industrial Hygiene Foundation we experience this gap, and we are constantly seeking a common denominator which will make possible a closer correlation of biologic results.

Extraneous factors in the cases of alleged occupational cardiac catastrophies complicate the studies. Certainly the changes in socio-economic conditions, which in many ways have improved man's health, have also had some deleterious effects because of our revised living habits, leisure time activities and especially our diet.

An important point is the fact that industry is recognizing the need to evaluate product ingredients before employees are exposed to them.

I thought you would like to know that the interest of the founders of Mellon Institute in humanitarian welfare extended to the field of cardiology. In 1914, Mr. R. B. Mellon established the Mellon Fellowship in Cardiology, and Dr. Andrew P. D'Zmura was chosen to go to London to aid in the construction of the first electrocardiograph. The following year, this instrument was brought to St. Francis Hospital here in Pittsburgh. The Fellowship was subsequently transferred to Magee Hospital where it continued until the year 1940 when it was absorbed into the residency program.

In the years since that time, industry has become increasingly aware of the opportunity it has for study and control of heart diseases among its workers. The industrial medical director is in a key position in promoting progress in this area of medical practice because the administration and management of cardiac cases at work is his responsibility. In addition, through the physical examination program he is often able to detect warning signals in time to prevent further damage. Industry, through its medical services and records, is also an excellent source of statistical data for epidemiologic studies covering a large segment of the population. In all these ways industry is contributing significantly

to the advancement of medical science in the study of heart diseases.

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Continued Employment of Individuals Partially Disabled by Heart Disease

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THE PHYSICIAN in industry has two major points of reference in considering the return of a cardiac patient to work. One is the patient's diagnosis and current health status. The second is the physical and emotional demands of the employee's regular job. In addition, there may be a number of contributory factors influencing his final decision, such as the patient's age, duration of disability, his motivation, home environment, and attitudes of management, fellow employees, and family physician.

DIAGNOSIS AND CLASSIFICATION

As he reviews the patient's medical record the doctor tends to categorize him into one of the following diagnostic and prognostic groups:[1–4]

ARTERIOSCLEROTIC HEART DISEASE

This is manifested by:

(a) *Coronary Insufficiency:* Properly treated angina is a controllable though recurrent disorder. In our experience about 85 per cent return to productive work, half of them with significant changes in job assignment.

(b) *Myocardial Infarction:* Mortality rates for various series may vary between 15 and 70 per cent.[5] Of those who survive a given attack between 55 and 70 per cent return to work. Approximately half will require some job change.

(c) *Congestive Heart Failure:* About 55 per cent will return to work, most of them with significant restrictions.

HYPERTENSIVE HEART DISEASE

This is manifested by:

(a) *Congestive Heart Failure:* Two out of three patients return to productive work, most of them with restrictions.

(b) *Diffuse Symptoms Ascribed to Essential Hypertension:* Practically all return to regular work. Where diastolic pressure is consistently over 120 mm Hg, climbing in unprotected areas or driving vehicles may be interdicted.

RHEUMATIC HEART DISEASE

This is manifested by:

(a) *Congestive Heart Failure:* About 60 per cent will respond to appropriate treatment and return to work. Over half of them will not be able to do their regular job because of restricted activity.

In addition, the doctor is aware that the individual under 55 years of age has a much better chance for successful placement than one above this age level. Employees with strong economic incentives (i.e., family responsibilities) or social ties to the group with whom they work will be less of a problem. Where the disability exceeds six months, the doctor's hopes of successful rehabilitation are not high. This usually means severe physical difficulty or a secondary emotional problem that is almost as resistant to treatment.

ENERGY DEMANDS OF THE JOB

As far as the demands of the job are concerned, the modern plant physician has a fairly accurate picture from his general knowledge of the plant environment of what a given assignment requires. Although the ultimate decision on returning a man to work belongs to management, the doctor's advice is influential. In special cases he may go to the job site, talk to the job supervisor, and observe work in

progress to be sure his estimate is correct. In some instances job analysis studies may have been done in the plant by an expert in this field, who has actually carried out the tasks required in different assignments. The following table, for example, illustrates the demands of a general laborer's job at the Baton Rouge Refinery.

TABLE I

Physical Demands of General Laborers' Jobs

		Hours per day		
		Maximum	Minimum	Average
Walking		4	1	2
Ascending stairs, etc.		1/2	0	1/5
Lifting and carrying	1 to 25 lb	8	0	5
	26 to 75 lb	3	0	1
	Over 75 lb	1/2	0	1/10

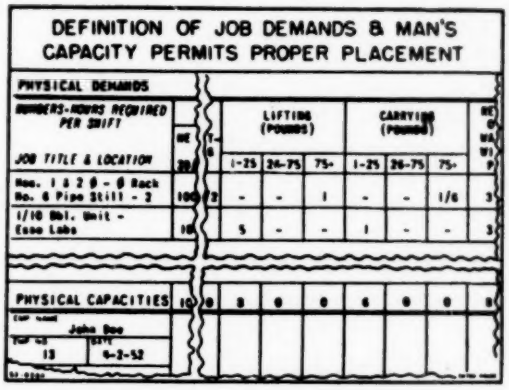
TABLE II

Capacities in Hours/Day Needed to do 90 Per Cent and 50 Per Cent of All Manual Labor Jobs (Skilled and Unskilled Included)

	Hours per day	
	90%	50%
Standing	6	4
Walking	3	1 1/2
Ascending stairs or ramps	1	1/5
Climbing (use of arms and legs)	1	1/5
Lifting up to 75 lb	2 1/2	1
Carrying up to 75 lb	1	1/5

Such studies have been of great educational value in demonstrating that many tasks require less physical effort than their titles would imply. Table II shows the capacities in hours per day needed to do 90 per cent and 50 per cent of all manual labor jobs at the same plant.

More exact studies of energy demands for various kinds of work have been carried out by Hellerstein and his group at Cleveland.[6] They confirm the above observation by showing that oxygen consumption for many so-called laboring jobs is only two or three times resting levels except for very short periods of time. These latter demands can be handled by many cardiac patients.


DEFINITION OF JOB DEMANDS & MAN'S CAPACITY PERMITS PROPER PLACEMENT

PHYSICAL DEMANDS

NUMBERS-HOURS REQUIRED PER SHIFT

JOB TITLE & LOCATION

LIFTING (POUNDS) 1-25 | 26-75 | 75+

CARRYING (POUNDS) 1-25 | 26-75 | 75+

Nos. 1 & 2 # - # Rock — 1-25: - | 26-75: - | 75+: 1 | 1-25: - | 26-75: - | 75+: 1/6 | 3

1/10 Bbl. Unit - Esso Labs — 1-25: 5 | 26-75: - | 75+: - | 1-25: 1 | 26-75: - | 75+: - | 3

PHYSICAL CAPACITIES — 8 | 3 | 0 | 0 | 4 | 0 | 0 | 8

John Doe — 4-2-52

Fig. 1. Physical demands and job analysis form

Physical capacities of the individual may be matched against the demands of various jobs by the use of analytical forms as shown in Figure 1.

The Physical Demands form is a re-statement of the Job Analyst's observation of specific types of effort for various process, mechanical, and semi-technical jobs. The Physical Capacities Analysis systematically lists the doctor's estimate of a given patient's ability to walk, lift, climb, etc., without disclosing diagnosis, prognosis, etc. These are useful guides for line foremen who may have to move men from day to day for optimum flexibility and efficiency.

Presumably, one could do the same thing on a research basis by measuring the cardiac reserve by the method of Levenson and his coworkers[7] and comparing it to the energy demands as estimated by Hellerstein's technic.

In a number of cases, no matter how much clinical information and job evaluation are available, the only way to determine whether or not a man can work is by a trial on the job. Sometimes this must be done in the face of minor anginal attacks or mild dyspnea. Although some risk is involved, trial at work is indicated if the health situation is stabilized, if the patient is anxious to work, has a realistic view of his

own situation, uses medication intelligently, and the occurrence of symptoms is as related to normal nonoccupational effort as it is to job effort.

At times the capacities of the individual match the demands of a number of jobs within the plant. Certain other variables, however, may complicate successful placement. Management may already be manning a number of jobs on a particular unit with restricted people. The addition of another man who cannot be utilized in certain emergencies may affect the overall efficiency of the operation. In such a situation they may feel unable to accept the individual under the conditions outlined by the doctor.

In some cases jobs which fit the limitations prescribed may be already occupied by able bodied men. Placement of the cardiac may mean that these men have to be moved to less desirable positions. Co-workers may sympathize with the cardiac's problems but not to the extent of agreeing to penalize themselves. In addition, there may be seniority rules which call for union agreement on the proposed move.

The attitude of the family physician may have an important bearing on placement. He may not agree completely with the plant physician's estimate of the situation. If rapport is not established between the two doctors, the patient may be torn between conflicting advice and develop additional uncertainty and anxiety.

The plant physician cannot solve these side issues unilaterally. One method which has been successful in Esso installations is the Placement Committee. Representatives of top plant management, line supervision, the Employee Relations and Medical Departments meet at frequent intervals to review problem cases. The medical story is presented in nontechnical terms without disclosure of confidential information. Problems involving management and employee interests are discussed and apparent conflicts often resolved. Cooperation of the private physician is secured by discussions with the industrial physician in which the work situation is more fully explained.

Summary

Successful placement of the cardiac in industry depends on skilled evaluation of his capabilities and the requirements of his job. Special problems of employee motivation, management and co-worker attitudes require tactful group handling. Mutual respect and understanding must exist between the physician in industry and his colleagues in private practice to insure the patient's enthusiastic participation.

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The Occurrence of Heart Disease among Industrial Workers

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IN ORDER to fulfill the presentation of the topic assigned to me, I shall discuss first the viewpoint of organized labor, particularly the policy of the International Ladies Garment Workers' Union, concerning the employment of the cardiac. The second phase of my discussion will be devoted to the occurrence of heart disease among older workers who have been in attendance at the Union Health Center for many years. This will be followed by material concerning the many cases of myocardial infarction which show benign characteristics not usually associated with this condition.

ORGANIZED LABOR'S VIEWPOINT

I do not speak for labor any more than the other industrial physicians on this panel speak for management in industry. However, since I was the Director of the only labor-sponsored medical service for many years, I have on various occasions explained labor's position in regard to handicapped workers and their employment.

Labor policies concerning handicapped persons seeking work in industry are clarified in recently published educational material issued by the AFL-CIO. In the booklet "*Jobs for the Handicapped*," local unions are advised to secure through collective bargaining the adoption of a planned policy for the physically handicapped, which should include contract provisions to safeguard their rights and guarantee equal treatment.

This booklet recommends the formation of union-management committees for the physically handicapped to solve the problems that arise through the re-employment of an injured worker after rehabilitation and also in the employment or transfer of workers with impaired health.

In attacking the problem of finding a job for a handicapped worker, a survey of the physical requirements of the job is essential so that selective placement is made possible. It is only for the purpose of selective placement that organized labor can countenance pre-employment or preplacement medical examinations. Such surveys determine the physical abilities of an individual so they can be matched with the physical requirements of the job and successful and permanent employment accomplished.

Inasmuch as selective placement is the key to successful employment of the handicapped, union-management committees can see that proper placement is achieved. It is understood that physically handicapped workers should be required to meet the same production and safety standards as other workers.

During the last decade the protective attitude of labor has been made clear through the hundreds of health and welfare contracts negotiated in practically every industry. The health and welfare contracts protect the worker by insurance coverage for medical needs; sometimes they provide direct medical service. More recently these benefits have been extended to the worker's family.

POLICY OF INTERNATIONAL LADIES GARMENT WORKERS' UNION

Good health is functional, and a productive worker is considered healthy. In the garment industry the union protects a man's job if he is ill, although another worker takes his place at his machine until he has had ample time to recover. Among the coat makers, if a worker who is ill becomes disabled and convinced that he cannot maintain production standards, he gives

up his machine and severance pay from the employer is arranged. In the crafts where severance pay is not available to the totally disabled worker, his job is held pending his return and it is not relinquished until his total and permanent disability is established.

CASE 20118 (Mr. J. S.) is an example: A 57-year-old cutter of heavy material used in manufacturing coats and suits, he suffered a cerebral vascular accident which resulted in a right-sided hemiplegia. He remained in the hospital for only nine days. After three months' convalescence at home he showed good recovery and went back to his job for two days. The employer found him not sufficiently productive and insisted that he take more time for recuperation. He returned five months later, but the employer still insisted he was not able to do the job satisfactorily. A medical evaluation was requested of us by the union.

Our records showed he had been our patient since 1933. In 1945 blood pressure was 190/120. In 1946 mild retinopathy developed; by 1954 he had grade III hypertensive retinopathy. Electrocardiograms were normal until 1950 when a tracing showed myocardial damage with left ventricular strain. Heart size by x-ray showed enlargement as early as 1951. Recently blood pressure readings were 260/130.

Upon our last examination in November 1956 it was felt that he had made satisfactory recovery from the hemiplegia with no loss of hand power, although he occasionally showed some slight drag of his left leg. However, it was felt that he could work only under special favorable conditions in which he would not be subjected to pressure. This case is being settled at the present time by the impartial chairman of the industry. It has serious social implications because of the worker's dependents. It will require tactful persuasion to have this worker claim total and permanent disability under the 1956 Amendment of the Social Security Law.

THE UNION HEALTH CENTER

The ladies garment industry employs 200,000 workers in New York City. The Union Health Center of the International Ladies Garment Workers' Union originated 43 years ago and has given medical service to garment workers on an ambulatory basis ever since, as well as supervising disability insurance, hospitalization, surgical and retirement insurance programs. Its primary objective is to help the workers maintain a state of health which will permit them to continue to work and be productive. Between 1,400 and 2,000 patients are seen daily in general medical, 20 different specialties, and the diagnostic services.

Prepaid medical service, emphasizing preventive medicine, has made possible frequent periodic physical examinations and the liberal use of diagnostic procedures at frequent intervals. In 1955 about 46,000 routine 70 mm chest films, 15,000 electrocardiograms, and about 100,000 laboratory tests were performed incident to medical examinations. This gives some concept of our screening procedures.

OCCURRENCE OF HEART DISEASE

A number of different phases of our work emphasize heart disease in this industry: the death rate, the examination of retirement applicants, the temporary and partial disability insurance program, and the program of case-finding and follow-up of serious conditions.

DEATHS FROM HEART DISEASE

Over 100 deaths per month are reported among the members of the International Ladies Garment Workers' Union eligible for union-sponsored life insurance. We find that 75 per cent of the members reported deceased had been in attendance at the Center at one time or another.

TABLE I

Deaths Among Members of International Ladies Garment Workers' Union in New York, N. Y.

Year	Deaths from all causes	Deaths due to heart disease	Per cent of deaths due to heart disease
1951	1,221	565	46.3
1952	1,356	664	48.9
1953	1,383	663	47.9
1954	1,434	608	42.4
1955	1,482	664	44.8
Total	6,876	3,164	46.0

When we scrutinize the death list that reaches the Center each month we find there has been an increase in the number of annual deaths from all causes and also from heart disease. Over the last five years 46 per cent of all deaths were caused by heart disease. Cancer follows heart disease as a leading cause of death, with 20 per cent of the deaths.

At the beginning of this five-year period, 1,221 deaths occurred. In 1955 a total of 1,482 deaths were recorded. The highest incidence of deaths from heart disease occurred in 1952: 48.9 per cent; the lowest point was reached in 1954 with 42.4 per cent.

RETIREMENT

During the year 1955, 185 out of 352 applicants for total and permanent disability retirement (52.5 per cent) were diagnosed as having diseases of the circulatory system. This included 14 per cent with intracranial disease of vascular origin. Of the 29 retirees who died during the first two years of retirement, 10 were cardiacs and six had intracranial disease of vascular origin.

SICKNESS INSURANCE

Heart disease caused the second longest period of disability among claimants for sickness insurance and was among the four highest causes of disability.

CASE FINDING BY ELECTROCARDIOGRAM

In the year 1955, 15,112 electrocardiograms were taken for 13,184 different individuals. While a large proportion of the patients have electrocardiograms taken year in and year out, some patients, for a variety of reasons, such as leaving the trade, lack of time to visit the Center, confining illness, or transfer to other cities, have a few year intervals between electrocardiograms. Below are the yearly totals of electrocardiograms for the years 1951–55 taken at the Union Health Center, New York, N. Y.:

1951	10,119
1952	10,329
1953	12,148
1954	12,533
1955	15,112

It is the policy of the institution to encourage periodic routine electrocardiograms for all individuals over 40 years of age. It is rare that patients in attendance for a cardiac complaint fail to have at least one or two electrocardiograms annually. Among the patients who have had electrocardiograms are many who have been referred to the Center by their private physicians for diagnostic procedures after being treated at home or in a hospital. They remain under the supervision of their private physician, although they return periodically for disability or check-up examinations at the Center.

TABLE II

Electrocardiograms per Individual in 1955

Number of Ecgs per individual	Number of patients	Number of Ecgs
1	11,613	11,613
2	1,295	2,590
3	215	645
4	47	188
5	9	45
6	4	24
7	1	7
Total	13,184	15,112

Among the 13,184 patients who had electrocardiograms, 3,202 showed abnormal findings. These were classified, for convenience, in three groups:

(1) Myocardial infarctions.
(2) Myocardial damage.
(3) Other abnormalities: arrhythmias, coronary insufficiency, left ventricular hypertrophy, right bundle branch block, inverted T in V_2 and V_3 in women.

The predominance of older workers in the industry explains the high incidence of arteriosclerotic heart disease in the patients who attend the Union Health Center. A study is under way of the 732 cases of myocardial infarction who attended the Center in 1955. Special studies are being done of 204 cases (classified as Type A, Table III) called back for

TABLE III

Categories of Electrocardiograms in 1955

Category	Number of patients		
Myocardial infarction		732	
Type A	204		
Type B	528		
Myocardial damage		1,703	
Other abnormalities		767	
Total abnormalities			3,202
Normal tracings			9,982
Total			13,184

re-examination during the preceding two months.

Type A-1 (Table IV) includes all cases that have had a myocardial infarction recorded for the first time in 1955, 73 of which have infarcts considered to be recent, that is, between one day and eight weeks old. These cases were all reviewed and reinterpreted by Dr. Marcel Goldenberg, our Chief Electrocardiographer. In addition to the typical electrocardiographic pattern of recent infarction, verification was made of a clinical episode by the medical history, except in the group of cases we will discuss later.

Type A-2 (Table IV) includes 64 cases showing myocardial infarction up to one year old, although it was recorded for the first time on an electrocardiogram taken at the Center during 1955. The third group (67 cases) includes patients whose electrocardiograms show myocardial infarction but who were not on the Register because of nonattendance for one or more years prior to 1955.

TABLE IV

Age of Myocardial Infarction at Diagnosis*

(204 Cases, Type A, Table III)

	Living patients	Deceased patients	Total	Per cent
(1) 1 day to 8 weeks	72	1	73	35.8
(2) 8 weeks to 1 year	62	2	64	31.3
(3) More than 1 year	62	5	67	32.9
Total	196	8	204	100.0

* Based on electrocardiographic pattern, confirmed by clinical findings.

You will note that 35.8 per cent of the 204 patients were found to have what we consider recent myocardial infarctions. Inasmuch as we operate an ambulatory clinic, the impression we wish to convey is that these patients actually visited the Center when the infarction was between one day to eight weeks old. In the last two groups we presume that the infarction was not recent.

AGE AND SEX OF INFARCTION PATIENTS

Table V shows that among the 732 cases, myocardial infarctions occurred predominantly in the 6th and 7th decades of life in both men and women. Among the men, 51 per cent occurred in the 60 to 69 age group and 30 per cent in men between 50 and 59 years of age. Similarly, in the women the largest number of infarcts occurred in the 7th decade of life and the next largest group of infarctions occurred in women in their fifties.

TABLE V

Age and Sex of Patients with Myocardial Infarctions

Age groups	Male	Per cent	Female	Per cent
70 and over	81	13.2	2	1.7
60 to 69	314	51.0	54	46.2
50 to 59	188	30.6	45	38.5
40 to 49	27	4.4	14	12.0
Under 40	5	0.8	2	1.6
Total	615	84.0	117	16.0

PLACE OF TREATMENT OF MYOCARDIAL INFARCTION PATIENTS

One-third of the infarction patients were treated at a hospital, one-third were ambulant, 24 per cent treated at home, while 11 per cent were treated by a private physician, presumably at home. (Table VI).

TABLE VI

Place of Treatment of Myocardial Infarction Patients

	Living patients	Deceased patients	Total	Per cent
Hospital	61	5	66	32.3
Home	48	1	49	24.0
Ambulant	63	2	65	31.9
Private Physician*	24	—	24	11.8
Total	196	8	204	100.0

* Presumably treated at home, but not as yet verified.

By the time this study was under way eight of these patients were deceased. This is men-

tioned merely as a point of interest, and is not a comment on the place in which treatment was rendered. It is natural to assume that the severest cases went to the hospital.

COMPLICATIONS

Among the 204 infarction cases studied there were 142 patients who had complications. Hypertension heads the list, followed by diabetes. A number of these patients had multiple complications. (Table VII).

RECOVERY FOLLOWING MYOCARDIAL INFARCTION

It is noteworthy that some garment workers continue on the job for years following infarction. The experience of seeing patients who have survived an initial infarction has become a common one, especially among physicians examining applicants for disability retirement during the last five years. It is not unusual to find evidence of two attacks in a patient.

TABLE VII

Myocardial Infarction with Complications

	Number of patients
Hypertension (25 had more than 1 complication)	62
Diabetes mellitus (16 had more than 1 complication)	31
Obesity (5 had more than 1 complication)	28
Anxiety state	14
Other (Hyperthyroidism, 1; Gall Bladder Disease 5; Gastric Cancer 1)	7
Total	142

AMBULATORY MYOCARDIAL INFARCTION PATIENTS

We have been greatly impressed by the fact that some of the patients who visited the Center year in and year out for treatment of a chronic illness, whose repeated electrocardiographic tracings were normal, suddenly show an electrocardiographic pattern of myocardial infarction. What is still more surprising is that many do not give a clinical history of a cardiac attack, and, upon examination, show little or no evidence of the expected serious picture of an infarction, in spite of the electrocardiographic pattern which points to recency.

Others, having complaints of chest pain, insist that they have had the symptoms for years, and are not convinced that because the electrocardiogram shows changes which point to myocardial infarction it is necessary for them to take special precautions, to follow medical advice and rest for a number of weeks before returning to work.

Still others make a return visit to the Center after a lapse of months or years and a routine electrocardiogram shows a pattern of an infarction, although previous tracings in their record during their earlier visits to the institution show no such evidence. The patient, upon careful questioning, gives no history to substantiate a heart attack. (Table VIII).

TABLE VIII

Special Study of 186 Cases of Infarction; Patients Alive and Working After Infarction

	Number of patients	Per cent
More than 21 years	2	1.0
16 to 20 years	4	2.7
11 to 15 years	14	7.5
6 to 10 years	66	35.4
3 to 5 years	38	20.2
2 years and less	45	24.1
Unknown	17	9.1
Total	186	100.0

This study, made last year, found that of 186 patients still working in the industry after an infarction, about 66 per cent had the heart attack more than three years previous. With Social Security benefits now available to totally and permanently disabled workers at age 50, there is a likelihood that the percentage of work continuance after an infarction may diminish.

Two cases are herein presented where the occurrence of an infarction was not supported by history and medical findings.

CASE 76213 (Mrs. S. W.). This 58-year-old female appeared at the Center on March 4, 1955 complaining of a recent cold and hoarseness, diagnosed as laryngitis. She was referred for routine electrocardiogram which showed a recent posterior wall infarction. Her last previous electrocardiogram in 1949 was normal.

Upon recall examination she could give no history of any symptoms referrable to an acute episode. She was working and completely asymptomatic. There was no palpitation, angina, or dyspnea. There were no cold sweats or vomiting. She had not lost any time from work in recent years and evidently had continued to work right through the time the infarction occurred.

CASE 85580 (Mr. H. R.). This 65-year-old male sewing machine operator gave a one-year history of substernal tightening on exertion. In March 1955 he sought medical care for a heavy cold because he also had weakness of the knees. He had had no medical attention since June 1952, when he was under treatment at the Center for hypertension. At that time the electrocardiogram showed chronic left ventricular strain.

At the March examination his pulse was 72 and regular, blood pressure was 200/110, and findings were negative as to heart and lungs with no evidence of congestive failure. After the electrocardiogram was completed, the paticnt was sent home routinely and told he would receive a report at the next examination.

The following day the electrocardiogram was interpreted as showing a recent anterior septal myocardial infarction. A letter was sent recalling the patient, but he did not respond because he had just moved and did not receive the letter. A second follow up reached him on April 19 when he returned for examination. He had continued to work without interruption.

He stated he had no special complaints and recalled no specific symptoms on repeated questioning. The second examination, four weeks later, revealed a pulse of 110, blood pressure of 220/100, weight 152, heart enlarged 2 cm outside midclavicular line, and diastolic gallop rhythm with occasional premature contractions. There was diminished resonance of the right base with a few fine, crepitant rales. The liver was not palpable; there was no edema of the extremities, and neck veins were flat.

The patient was willing to discontinue work for the time being since the working season was coming to an end. The electrocardiographic findings indicated that the infarction occurred recently, but it was difficult to secure any specific information from him about symptoms which might date the incident accurately. Apparently it occurred during a heavy cold at the time when he had weakness of the knees.

Apparently many of these older workers are relatively insensitive to mild symptoms of coronary disease. Therefore it is only through intensive questioning that the electrocardiographic findings of myocardial infarction can be substantiated by some symptoms that would hint of a history of an infarction.

The seasonal nature of the ladies garment industry, as well as the fact that many of the crafts are sedentary, plays a part in deterring workers from seeking medical care except for severe complaints during the two busy seasons of 12 to 15 weeks. As a result many workers come in for medical attention long after the mild coronary episode may have occurred. The nature of the industry also provides a suitable atmosphere for workers to become so engrossed in producing enough in the short working season to secure income for the year that they tend to ignore mild symptoms of any disease. They are too tired to seek medical attention after work and cannot afford to take time off during the day and lose income, being paid on a basis of piecework.

The accumulated evidence emphasizes that a large number of workers have a form of benign coronary disease with myocardial infarction which evidently occurs mostly in older age groups and carries with it a not unfavorable outlook for continued employment.

Apparently we meet a type of myocardial infarction that either involves a small area or else the infarction develops slowly. Moreover, because of the age of the patient, he is likely to have a good collateral circulation. Frequently symptoms are vague and atypical, such as heartburn, pain in the jaws, nausea without vomiting, a light abdominal pain, gaseous eructation. An infarction is discovered only through routine electrocardiography. These cases seem quite different from the acute type of myocardial infarction with shock, or the subacute type with severe pain and other symptoms which result in a period of serious illness and confinement.

SUMMARY

Benign coronary disease occurs not infrequently among the patients of the Union Health Center which provides ambulatory medical services to 200,000 workers employed in the ladies garment industry in New York City.

A study of 204 cases of myocardial infarction discovered in 1955 shows that 35.8 per cent of the infarcts were between one day and eight

weeks old when the electrocardiogram was performed at this ambulatory clinic.

One-third of the cases had been treated in the hospital, one-third at home, and one-third on an ambulatory basis.

Some patients who had visited the Center for treatment of chronic illness and whose numerous electrocardiographic tracings taken over a period of years were normal, suddenly showed a pattern of myocardial infarction. Some did not give clinical histories of a recognizable cardiac attack and upon medical examination showed little evidence of the expected serious picture of an infarction. Many of the workers had come in for medical attention long after the mild coronary episode may have occurred.

The accumulated evidence emphasizes that many workers have a form of benign coronary disease with myocardial infarction in which the typical history, symptoms and signs are absent, hidden or obscure. Such infarctions evidently occur among older age persons and carry a not unfavorable outlook for continued employment.

Apparently we meet a type of myocardial infarction that either involves a small area or else the infarction develops slowly in older persons with good collateral circulation. Routine electrocardiography of patients is responsible for uncovering some myocardial infarctions. Some of these cases have no record of an acute episode with shock, or the subacute type with severe pain and other symptoms, which result in periods of serious illness and confinement in the hospital.

Heart Disease in Industry and the Role of Organized Medicine

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AMONG the leading chronic diseases are the cardiovascular disorders. Such ailments are estimated to be responsible for 700,000 new victims each year.[1] The prevention of the degenerative arterial disorders, which afflict the bulk of such patients has, to date, met with no striking success. In fact, our aging population has brought an increase in the number of patients with vascular disease. Through the kindness of natural restorative processes, our therapeutic efforts fortunately promote varying degrees of rehabilitation in these patients. To what extent can these men and women contribute to our economy?

A physician knows that all men and women fall short of their maximal usefulness. Bluntly, we are all physically, mentally, or emotionally handicapped to some degree. Our objective, therefore, is to match the productive capacities of our people to the work needs of the world. Rare is the person who cannot contribute something if he is sufficiently motivated and if his abilities are harnessed. The role of organized medicine is obvious. It is to bring the art and science of medicine to the support of the will, the ability, and the opportunity to engage in useful work. The role has proved not to be a simple one in a society which specializes in creating work strait jackets and factitious devices whereby one may subsist without working!

IS WORK HARMFUL?

Garnett[2] observed: "Since about 1932, there has been a growing acceptance of a philosophy by many segments of our civilization to the effect that work in general is harmful. Even we as physicians are prone to attribute many of our daily aches and pains to overwork and stress and strain. While this may be true in a limited sense, the continuation of such a philosophy can and will lead to our downfall as a civilization. The growth and acceptance of this philosophy have unquestionably caused more people to assume that the cause, development, and aggravation of some diseases were brought on solely because they had to work for a living. They seem to labor under the delusion that, were they financially endowed from the cradle, there would be no grave. This, of course, is not true. We know that abrupt and sometimes unnecessary retirement causes an early and untimely demise, and the medical profession as a whole is attempting to keep more and more people gainfully employed over a greater span of life. I have no solution or suggestion as to how to combat this insidiously spreading philosophy, but we as physicians should be on guard lest we encourage it by inadvertently insinuating or suggesting that work *per se* is to be condemned. We should look upon our daily chores and our occupation, whether we are self-employed or work for others, as a God-given chance to produce and to justify our existence. To do otherwise is contrary to the basic law of nature that prolonged disuse of any organ or structure of the body results in disease."

There appears to be a need to reaffirm the point of view that work is a normal part of human life, not unlike eating, sleeping, adolescence, pregnancy, and senescence. Cardiologists do not consider work to be a cause of coronary artery disease, hypertension, rheumatic carditis, or in fact any type of heart disease.[3–5] Our medical cogitations are fouled by the juridical concern for aggravating or abetting factors bearing upon the *manifestation* of heart disease.[6,7]

Having identified the presence of degenerative vascular disease in a worker, there is, at times, a tendency for us to forget the natural history of disease, to wander away from the base of medical prognosis and start looking for ghosts. Do we have the clairvoyance to identify such specters? Myocardial infarction in the industrial worker, for example, is not infrequently an unrecognized episode and one with a better prognosis than some hospital statistics indicate.[8] With proper job placement and satisfactory mental and emotional adjustment the outlook for the worker with degenerative vascular disease is equal to or better than that of the man who ceases work immediately upon recognition of his disease. Persons who have heart disease of slight to moderate severity are almost always capable of undertaking useful work.[9]

Work Barrier

Physicians have a grave responsibility in the verification of heart disease. There are workers who have perfectly normal hearts who mistakenly believe they have heart disease. Other persons have functionally harmless forms of heart disease which cause no actual disability. We must acknowledge the psychologic, sociologic, and motivation needs of the unemployed man with some degree of heart disease. It has been suggested that fully one-fourth of the latter category of patients are not working because of either "an unwarranted fear on the part of the patient or the fact that the patient uses his heart disease as a means of avoiding work or gaining financial compensation."[9] Can our profession face this situation squarely and derive the correct answer for each individual patient-worker who now lives and works under such plans as the cash disability benefit provision of the Society Security Amendments of 1956?

Unemployment based on a desire to avoid work is a serious challenge. Its growth can result in enormous financial loss to the nation, in gross deterioration of the integrity and creativity of our fellow men, and in unwarranted hardships on their families.

Kline[10] noted that formerly there was a lack of general acceptance of an ability to work in men with heart disease. His recent survey indicated that this is no longer true, at least in industries with medical departments. Instead, the chief bar to employment is the threat of compensation claims arising out of alleged aggravation of pre-existing heart disease.

A review of employment policies and practices in the Boston area indicated that about half of 100 employers in the survey excluded patients with cardiac disease from new employment.[11] The potential risk of workmen's compensation costs was given as the primary deterrent to such employment. Other deterrents were the lack of suitable jobs and added costs of sickness benefit plans.

It is apparent from this and other reports that employers are prone to continue in employment those workers who develop cardiac disabilities during their employment. Olshansky and his associates[11] found that of 347 disabilities due to heart disease, reported by 84 employers as occurring during the year previous to their survey, 80 per cent of the workers were returned to employment.

Guide lines on rehabilitation objectives, technics, and accomplishments for heart disease have been furnished by those who have made special studies of the technical aspects of medicine's contribution to this type of disability.[10, 12]

One group concerned with rehabilitation reported that 45 per cent of patients referred in the II-C to III-C (functional-therapeutic) classification were able to return to normal work activity.[10] The rate of rehabilitation decreased with age. Symptoms which appeared to the patient as evidence of his disability were often unrelated to the organic heart condition. "The social and psychologic condition of the patient, his motivation and interest, are frequently much greater determinants for success in rehabilitation than the extent of his organic heart disease, or even the amount of superimposed psychosomatic symptoms."[13]

Problem of Liability and Compensation

There are employers who, for good reason, are afraid of uncertain and severe compensation costs which may result from the employment of workers with heart disease. Ungerleider[14] has stated: "The real crux of the problem of heart disease in industry is the question of liability and

compensation, and here the fears of the employer have a substantial basis." Goldwater and Weiss reported that in New York State Workmen's Compensation, payments for heart disease amount to about two million dollars annually and account for nearly 4 per cent of all compensation costs. Ungerleider believes "unwise legislation enacted without the benefit of sound medical knowledge has resulted in a disservice to industry and employes alike."

Some compensation awards in this area have been substantial in amount but poorly substantiated by competent medical opinion, I am told. I must say at this point that I have had occasion to examine the facts of a few decisions of compensation commissions which received considerable criticism from the "Monday morning quarterbacks." In most instances I found the record to show either (a) inept, improper, or unclear medical testimony, or (b) a poorly defended case (attorney failure) leaving the hearing officer no alternative to his decision under the acts governing his office.

Beard and his associates[15] reported that medical review of decisions by the California Industrial Accident Commission, in suitably documented records of heart disease claims, yielded agreement in 64 per cent of the cases. This figure may assume greater significance by virtue of the further finding that a second review by a previous reviewing physician of 101 case abstracts showed that the physicians agreed with their own previous decisions in only 70 per cent of the cases.

Without attempting to define either the enormity of the employer's risk or the extent of improper decisions by compensation commissions we can, I hope, agree that organized medicine has a responsibility to work with all groups interested in protecting the rights of the worker with heart disease, his rights to be productive as well as his derived rights under disability of whatever origin. Medicine has a role in evaluating correctly the worker's abilities as well as his disabilities, in acquainting industry (labor and management) with the worker's potential, and in aiding the agencies responsible for evaluating the legal considerations.

An all out effort by all parties concerned is forced on us because our economy simply cannot afford the loss of production or the expense of retiring from work a large proportion of our ten million or more patients with cardiovascular disease.[16] We must find a rational and workable common meeting ground for the worker, his labor leadership, industrial management, and State and Federal governing agencies. We must look also to the education of physicians for the part they play in these activities.

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Program of the United States Public Health Service in Heart Disease in Industry*

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IN 1948, Congress passed the National Heart Act which outlined the general basis for the overall program of the Public Health Service in heart disease. The express purpose of the Act was "to improve the health of the people of the United States through the conduct of researches, investigations, experiments, and demonstrations relating to the cause, prevention, and methods of diagnosis and treatment of diseases of the heart and circulation; assist and foster such researches and other activities by Public and private agencies, and promote the coordination of all such researches and activities and the useful application of their results; provide training in matters relating to heart diseases, including refresher courses for physicians; and develop and assist States and other agencies in the use of the most effective methods of prevention, diagnosis, and treatment of heart diseases."

The important impact of the cardiovascular diseases cannot be ignored. They result in more than 800,000 deaths each year, accounting for over half of deaths from all causes in this country.

The prevalence of heart disease in the general population is not accurately known. In a Public Health Service study that is in progress in Framingham, Massachusetts, it has been found that 9.3 per cent of a random sample of the adults, age 30 to 59, had definite evidence of heart disease. A study by the Chronic Illness Commission has found that 12.2 per cent of a random sample of adults, age 35 to 64, in Baltimore had evidence of definite heart disease. It is hard to say what proportion of employed persons have heart disease, but from the results of various studies it would appear that a conservative estimate would be that at least 5 per cent of the working population has some form of heart disease.

It has recently been estimated that 653,000 man-years are lost each year as a result of the cardiovascular diseases. This loss in man-years from these diseases in 1953 is the equivalent to a loss of $2,468,340,000 in earnings alone.

There are many aspects of the Public Health Service programs which bear directly or indirectly on the problem of the cardiac in industry. I think it should be pointed out here that the Public Health Service is interested in the total spectrum of the heart disease problem ranging from prevention and proper recognition of the disease when it exists, to the prevention and limitation of disability and restoration of the individual to a useful life. In many of these, we are working hand in hand with other constituents of the Department of Health, Education, and Welfare, mainly the Children's Bureau and the Office of Vocational Rehabilitation.

Our progress and success in meeting the problem of the cardiac in industry are going to depend on our acquiring more knowledge than we now have. This calls for research. The research arm of the Public Health Service is the National Institutes of Health and for cardiovascular diseases, it is the National Heart Institute. This Institute is carrying out an extensive research program both in the research conducted at the National Heart Institute in Bethesda, Maryland, and through the sup-

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port of research in universities and medical centers throughout the country. From 1949 to the present time, 4,643 research grant awards have been made totaling $53,380,259. Supplementing the research program, the National Heart Institute also supports the training of research workers representing a wide variety of disciplines in the training centers of the nation. Since the Heart Institute was founded in 1948 2,574 fellowships and traineeships have been supported totaling $21,267,653.

Naturally, most research is aimed at understanding the etiology of these diseases. In addition, however, research studies are now exploring the relationship between work and the development of heart disease; how best to measure the residual work capacity of the diseased heart, and how to relate the reserve capacity to the job demand. These studies have immediate bearing on the problems of the cardiac in industry.

Heart Disease Control Program

In addition to the research that is supported through the National Institutes of Health, the Public Health Service assists the States in providing health services to the people of the United States. This function is the responsibility of another arm of the Public Health Service, the Bureau of State Services. Within the Bureau, the Division of Special Health Services, of which I have had the pleasure of recently being appointed the director, is concerned with adult health problems and the maintenance of adult health as it relates to his environment and society. This includes a variety of programs which contribute primarily toward the health maintenance of our adult population. Among these programs is the Heart Disease Control Program in which two general areas are being developed:

(1) *Research:* The kind of research is needed which will translate the products of laboratory research to practical application or the epidemiologic type of research in which the place where people live and work is the laboratory itself.

(2) *Services:* Those services are to be provided which are necessary in a community or industry to aid the physician in meeting the total needs of his cardiovascular patients.

Research

Energy Requirement Studies: An example of the types of research conducted by the Heart Disease Control Program which is related to the cardiac in industry problem is a study recently conducted at the Lockheed Aircraft Plant in Los Angeles.

One of the pressing problems which concerns the physician when confronted by an individual with newly diagnosed cardiovascular disease is the recommendation that he should give as to future employment of the individual. This requires that the physician be able to assess the cardiac reserve of the patient. Also required is a knowledge of the energy demands of the job being considered for the individual. The study at Lockheed was aimed at determining whether it was possible to classify jobs by measuring the energy requirement. This was shown to be possible. Second, since the energy requirements of the jobs were done on normal individuals, it was necessary to find out if cardiacs and noncardiacs require the same amount of energy when doing the same job. This was also shown to be so. The results of this study, which are now being confirmed by others, give encouragement that useful and practical tools will be developed to measure the work tolerance of cardiac patients as well as the energy requirements of specific industrial jobs. This potentially will be helpful to the practicing physician and the industrial physician.

Epidemiologic Studies: Another example of research conducted by the Heart Disease Control Program is in the epidemiologic area. This may contribute information that will influence the cardiac in industry. An attempt is being made to verify the observations in England of Dr. J. N. Morris who found that workers in less physically active occupations have more severe coronary heart disease than do comparable workers in more active occupations. It has also been stated that fewer farmers suffer from heart disease than do white collar workers. It is anticipated that a specific study now being carried on with the cooperation of the medical society, physicians, and health department of North Dakota will reveal whether or not farmers have a lower incidence of clinically manifest coronary heart disease than do nonfarmers

within a defined population of North Dakota. Correlations between the incidence of coronary heart disease and such characteristics as physical exercise, smoking, diet, height-weight, and ethnic origin are also part of this study. Another similar study in a more industrialized area is currently being planned in Middlesex County, Connecticut, to determine the incidence of coronary heart disease before a large industrial plant opens in that county, and then to measure whether any change occurs after the plant opens.

Studies such as these can only be conducted with the full cooperation of the practicing physician. We are gratified to see the interest physicians are showing in these studies in their communities. Industry is peculiarly suited to conduct similar studies because of the close observation that is possible in stable industrial populations. This permits the opportunity to observe and learn more about the onset and course of cardiovascular disease under a variety of environmental conditions.

Case-Finding: Another area of direct interest to private practitioners and industrial physicians which is carried on by the Heart Disease Control Program is the development and evaluation of case-finding procedures. It would be extremely useful to the industrial physician with a limited staff to be able to apply a few screening procedures to the workers he is serving, and thereby detect a large proportion of the heart disease rapidly, economically, and with a high degree of employee acceptance. He would be able, then, to detect heart disease earlier and consequently be better able to supply health supervision which would maintain the individual's health at an optimal level. Practical screening tests for heart disease are already available; however, further studies are being made to improve their effectiveness.

Health Services

You will recall that I said two general areas were being developed in the Heart Disease Control Program and until now I have dwelt on the research programs. Now I would like to move on to the second area being developed—health services.

The cardiac patient is a complex creature with a mind, body, and emotions and in addition to that he is influenced by his job, his family, and the society in which he lives. No community can neglect the total needs of the individual who has heart disease if he is to forestall the disabling consequences of the disease. The Public Health Service assists communities in developing services which are needed to meet the community needs of cardiac patients by providing grants-in-aid to the several states and also providing technical assistance and guidance to states and communities in development of these services.

Community Nursing Services: What are some of these services which affect the cardiac in industry? The first, I think, are community nursing services which assist the physician by teaching the family how to provide needed services for the cardiac patient and hasten his return to employment.

For example, in many communities, on request of the practising physician, the public health nurses visit his cardiac patients in the home or even in industries where cardiacs are employed and give mercurial diuretics, thereby allowing the worker to continue in employment and remain free of decompensation. In addition, home nursing may relieve a situation so that the wage earner can continue employment instead of staying home and caring for the cardiac patient.

Work Classification Units: Another service which is developing in communities and has a direct bearing on the cardiac in industry is the establishment of work classification units. These units involve the team-work of physicians, social workers, and vocational counsellors who determine the suitability of cardiacs for specific jobs, attempt to find such jobs, and maintain follow-up services as needed. Units of this type also serve as research centers for studying the relationships of heart disease and employment. There were, at my latest count, 42 of these units scattered throughout the country. These units have found that approximately 75 per cent of the workers with cardiac conditions evaluated can be returned to productive employment.

I have mentioned the work classification units not because of the numbers of persons who received their services, but because they

have, through focusing their attention principally on the occupational potentialities of the cardiac patient, brought about a new way of looking at the person with cardiovascular disease, in a more or less clinical setting. In addition, they have brought to the attention of all physicians and researchers the gaps in our knowledge which need to be filled before a cardiac patient's work capacity can be properly evaluated and the person properly placed in a type of job suited to his cardiac status.

There are other types of services that the Public Health Service is assisting states and communities to develop and establish. Many of these services, such as prevention programs in rheumatic fever, case-finding programs, and provision of nutrition services, render indirect benefits to the cardiac in industry.

Summary

There are many aspects of the Public Health Service programs which bear directly or indirectly on the problem of the cardiac in industry. The programs are aimed at the total spectrum of the heart disease problem ranging from prevention and proper recognition of the disease when it exists, to the prevention and limitation of disability. These are being projected as programs in research, education, and community services.

Rehabilitation of the Cardiac

Introduction to the General Problem

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UNTIL QUITE recently, the skills of the physician were directed primarily at the treatment and cure of physical illness. The care of the mental patient was little better than it was in the Middle Ages. The prevention of disease was given very little consideration. The rehabilitation of the sick and the injured was almost wholly neglected. The mentally ill, the misfit, and the seemingly physically incapacitated were all compelled to shift for themselves.

But the period of enlightenment ultimately arrived. The mental well being of an individual came to be considered as important as his physical health. The corpus sanum was recognized as an integral component of the mens sana. The god of healing opened both his eyes.

Almost simultaneously with the awakening of medicine from its earlier torpor, came the era of industrial expansion, with its limitless production and its unrestrained competition. The machine age had arrived. No person was any longer self-sufficient. Each became more and more dependent on the other. Each worker was, of necessity, compelled to vie with the others, in order to obtain employment and to survive. Special aptitudes and technics and skills had to be developed through many years of study and application.

The loss or diminution of these acquired skills as a result of disease or injury or increasing age, deprives the affected individual of an essential prerequisite for earning his livelihood and for maintaining his physical and mental well being. It deprives society, also, of the fruits of these skills. For industry suffers more through the impairment of a workers' health and the loss of his talents than through the breakdown of a machine. The machine can easily be replaced. The skilled workingman cannot. To overcome this loss of special skills, due to injury or disease, by improving the function of the affected parts or by minimizing the effects of the causative condition, is the aim of Rehabilitation Medicine.

Relatively few patients are permanently, totally disabled. The great majority of patients have a partial disability, either temporary or permanent. It is essential, therefore, that the patient's attention be focused on his residual capabilities rather than on his irreparable disabilities, and that these residual capabilities be further developed constantly. Through rehabilitation in medicine, an attempt is made to restore to a handicapped person, as far as is possible, his maximum physical, mental, and vocational capacities.

In order to achieve this, it is essential there be the thoughtful cooperation of the physician with specialists in diverse fields, medicine, psychiatry, surgery, social service, physiotherapy, as well as assistance of special teachers, of employers, and of government.

"Each of us," it is said, "is an impregnable fortress, which can be laid waste only from within." Unemployment and idleness—especially unnecessarily enforced idleness—are among the more important destructive factors. They produce personal and familial debasement, due to the resultant worry and want and privation. Self esteem is too frequently lost, and morale too often broken.

The physician and the patient's family are, in many cases, responsible for this needlessly enforced inactivity. Commonly, as in cardiac

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disease, the physical disability is not of overwhelming significance. But the fear of heart disease and of its dread consequences, thoughtlessly inspired by the attending physician, and carefully nurtured by the patient, his wife, and his children, is the important cause of the assumed disability and the enforced—the unnecessarily enforced—idleness.

Attention should never, therefore, be focused solely on the existent heart condition. The physician must treat the victim, and not the disease only. Since most workingmen can understand simply expressed facts concerning their disease, its outlook, and the rehabilitation treatment to be undertaken, these facts should be clearly stated, as soon as it seems wise to do so, and in as optimistic a manner as is commensurate with the existent conditions. "For correction does much to improve the state of man, but encouragement is often more effective."

PHYSICAL REHABILITATION

Physical rehabilitation should be considered whenever, in the opinion of the physician, an improvable physical disability exists, whether it is of congenital origin, the result of traumatic or non-traumatic disease, or due to the aging process. It should be instituted as soon as is safely possible after the physical incapacity appears, since the success of rehabilitation treatment is, in great part, dependent upon the active, voluntary cooperation of the patient, and since a prolonged period of idleness tends to produce a spirit of hopeless resignation and a hostile mental attitude, which make rehabilitation therapy inefficacious.

Too early attempts at physical rehabilitation, however, are unwise, for they may aggravate the existent disease and jeopardize the success of any future treatment. The physician's experience, his clinical acumen, and his sound judgment will determine the optimum time for the institution of the treatment. It is generally considered much better to have a living physical and psychologic cripple, than an almost rehabilitated corpse.

MENTAL REHABILITATION

Should the incapacity result from some mental disturbance, without organic physical involvement, or with a minor physical involvement which is grossly exaggerated, rehabilitative measures should be focused on the more important mental outlook of the patient. The fears and hopes and feelings and longings of each person are peculiar to him, and can be expressed and described only rarely. Occasionally, it may be possible to convey some inkling of these idiosyncratic sensations to a stranger. In the rehabilitation of such patients, the doctor must seek to open wide the means of communication between himself and the patient. For only thus can cares and fears be released and dispersed. The psychiatrist, the general practitioner, and the priest confessor are among the few who can achieve this end. Failing this, the rehabilitative treatment of the mentally disabled is too often unsuccessful.

This physical and mental rehabilitation aims at the ultimate complete or partial restoration of the skills lost, due to injury or disease, and at the consequent complete or partial restoration of the patient to his previous calling.

VOCATIONAL REHABILITATION

Should the physical condition of the individual be irreparable, however, and cause a permanent, total loss of his acquired skills, the aim of rehabilitation is re-education, in the hope that some related or unrelated work may be found, which is willingly undertaken and maximally gratifying. This is vocational guidance. It rests upon the concept that both education and occupation promote the efficient and happy life of the individual. Vocational guidance is an essential component of rehabilitation treatment, but has not, unfortunately, received as much attention from physicians as its importance merits.

Each person interprets reality in his individual way. The acceptance or rejection of reality, in its individually varied and diverse modifications, accounts, in great part, for many of the seemingly insuperable hardships endured by man. The rehabilitation process seeks to reestablish reality as reality. It aims to banish imagined fears and false interpretations. It strives to emphasize ability and to de-emphasize disability. It encourages the patient to face the truth bravely, and to accept it hopefully.

The duty devolving on the physician is great.

He must, at the appropriate time, suggest a retraining program for those disabled patients who can regain their lost skills, or a re-education program for those whose skills are permanently lost, and who must, therefore, acquire new skills at new jobs.

FACTORS IN SUCCESSFUL REHABILITATION

The success of the rehabilitation treatment extended to any particular cardiac patient depends upon many factors. Among the more important of these are: (1) The type of heart disease present; (2) the duration of the condition; (3) the degree of functional superimposition; (4) the length of inactivity prior to the initiation of the treatment or the institution of vocational guidance; (5) the willingness of the patient to cooperate fully with the doctors; (6) the attitude of the patient's family; (7) the knowledge and skill and experience of the attending physician, and the adequacy of the treatment given; (8) the assistance and cooperation of employers and the State; (9) the availability of cardiac work classification units, sheltered workshops, and other similar aids.

What rehabilitation treatment has already done is very praiseworthy. What it can accomplish further depends, in great part, on the general practitioner and internist and on their willingness to learn a new and valuable method of therapy. With their cooperation, the outlook for a wide expansion of physical, mental, and vocational rehabilitation will be very good.

Job Evaluation for the Cardiac in Industry

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I HAVE BEEN asked to discuss the question most commonly asked by convalescent cardiac patients. "Just what kind of work can I do?"

It is a rarity, nowadays, to find a heart patient who is satisfied with simple time-honored statements, such as: "Request a transfer to a lighter job." "You've had a heart attack, but there's nothing the matter with you now, go back to your regular work and take it easy." Nor can the heart patient be pacified with the commemorative chronicals of courageous men and women who have overcome physical handicaps to become successful.

The modern heart patient is indoctrinated through newspapers, magazines, radios, and books in matters pertaining to rehabilitation. During his convalescence, well-meaning friends and relatives have bombarded him with advice and with literature which, on the one hand, stress the desirability of his being idle and resting, emphasize the danger and destructiveness of work, and advise the reading of books in order to live longer. On the other hand, these same relatives and friends insist upon his ability to work, urge his return to work so that he may be a useful member of society and not a burden, and stress work as nature's best medicine. So the cardiac patient's knowledge of the rehabilitation of the cardiac is greater and, perhaps, more confusing than his physician suspects.

To the modern heart patient, his rehabilitation means his physical, mental, and social adjustment. To attain such a status, he expects a variety of services: medical care, psychology, psychiatry, physical therapy, social service, recreation, financial aid, counseling and guidance, vocational training, selective job placement, and follow-up of his progress.

Not only that, but he has read somewhere that one of the chief causes of the increase of chronic disease is the great advance made in diagnosis and in medical care which has delayed death and produced an aging population. He has also heard that medicine has no specific answers to his problems of diseases of the heart and circulation and that medicine, therefore, has to resort to the varied specialties of rehabilitation in order to teach him to live within the limits of his disability and to the utmost of his capabilities. He may, indeed, somewhat resentfully perhaps, hold his physician directly responsible for his longevity, and expect his physician, therefore, to direct him to successful employment regardless of his capabilities.

In any event, here he is: our modern heart patient. He has been propagandized about the work ability of cardiacs; he has been told that his "energy cost" is practically the same as that of healthy individuals; he has been informed that there are numerous jobs that a cardiac can do; and he is depressed, disappointed and disillusioned at not being able to find work, despite the recent headline in the *New York Times*, "Many Jobs Suited for Cardiacs."

APPROACH TO THE PATIENT

How shall we handle our poor patient? What shall we tell him when he asks: "Just what kind of work can I do"?

Because of the possibly disorderly and indefinite indoctrination to rehabilitation that the

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patient already has had, it seems to me that we should avoid ambiguity, that we should be very specific in our recommendations, and that we should have a particular, individual work formula to give the patient, even though it be based on arbitrary principles.

During or directly after an acute episode such as coronary occlusion, an attack of congestive failure, or a bout of acute rheumatic fever, a guarded, short-range program should be discussed with the patient. It is necessary, first, to explain to him the cause and nature of his particular disease; to describe the extent to which his organic heart disease contributes to his symptoms and disability; to review the physical examination and laboratory findings. In so doing, injudicious comment or incomplete explanation should be avoided, for that may increase anxiety and tension, or precipitate a cardiac neurosis.

Symptoms caused by prolonged anxiety and tension should be evaluated. It should be pointed out that each symptom is not caused by heart disease itself. Additional physical defects and the existence of organic disease other than heart disease must, similarly, be evaluated for the patient. During this phase no one aspect of the patient's symptomatology should be over-emphasized. Under no circumstances should the patient be told that he can never again do his regular work. You must remember that the patient can only absorb so much of what you tell him at one sitting. It is far better to extend the evaluation over several interviews, and, at the same time, build up the patient's morale, by outlining a minimal, temporary activity program for him. Only when you, the attending physician, are convinced that the cardiac lesion has been stabilized, should you discuss the patient's employability and his return to work.

Evaluation of Cardiac Function and Work Capacity

The stability of the patient's functional capacity is determined chiefly by clinical judgment. In evaluating his cardiac status, one should take the following clinical factors into consideration: (1) The etiology of the cardiac condition; (2) the nature of the pathologic changes; (3) the disturbances in rhythm; (4) abnormal fluctuations in blood pressure; (5) the signs and symptoms of diminished cardiac reserve; (6) the chronology of previous cardiac episodes and the prognosis of the possibility of recurrence.

When the patient's cardiac lesion and his functional capacity have become stable, one should estimate his work capacity. The familiar cardiac function tests, such as the Schneider Index, the Master Two-Step Test, Levy's Anoxia Test, and their modifications, appear to be of little or no value in measuring physical capacity or work tolerance. Evaluation of the patient's work capacity must be based, chiefly, on other factors. These factors are many. Among them, of course, are the diagnosis of the condition and the treatment required. They are never quite the same in any two cases.

The same criteria used in deciding whether or not the patient's cardiac lesion was stable, also determine his work capacity. The etiology of the heart disease is of prime importance, as is the nature of the pathological change in the heart.

Rheumatic Heart Disease: Chronic valvular disease occurs on the basis of subacute or chronic infectious endocarditis; it can be congenital, rheumatic, luetic, or arteriosclerotic in origin. Cardiovascular syphilis is rapidly disappearing because of the use of penicillin. Infectious endocarditis has been reported to be 90 per cent curable. The life expectancy of the rheumatic is still apt to be short, depending on the amount of valvular deformity and the severity of the initial myocardial involvement. The hazard of recurrent rheumatic activity has been lessened by the prophylactic use of antibiotics. Current surgery of the heart seems to prophesy the increase of the physical fitness and working ability of the rheumatic patient, as well as of the one suffering with congenital heart disease.

How shall we advise the young rheumatic patient concerning his occupational training? Shall we recommend that he continue at a strenuous, well-paying occupation which he likes and which does not disturb him at present, or should we advise retraining in an occupation

in which he can engage, despite a later recurrence of the rheumatic activity or the development of mitral stenosis?

At a recent meeting of industrial physicians, one of my colleagues confided to me that his firm had changed its policy of not employing people who had rheumatic heart disease. It now does hire such people but with two qualifications. They must be females, and they must be young and pretty. For his firm felt that it could reasonably expect young, pretty females to be married within several years after they began to work and so could not possibly endanger themselves nor their employer, in so far as their hearts were concerned.

Incidentally, the condition of the labor market, whether it be hard or soft, will determine, to a great extent, if a patient will or will not get a job. I have visited plants at periods of peak employment, and have seen the recruiting activities of personnel departments. I have seen them actually canvass for employees from door to door in industrial communities. Of course the presence of heart disease in the potential worker was not even considered.

Congenital Heart Disease: The incidence of congenital heart disease is small, perhaps one per cent of all organic heart disease, in all age groups. Death occurs in infancy usually or in early childhood and adolescence. The life expectancy is, in any event, short. Our advice for the occupational training of patients with congenital heart disease is apt to be philosophical and academic, rather than based on the currently accepted principles of rehabilitation.

It seems, then, that our greatest problem is that the rehabilitation of the cardiac, i.e., his restoration to mental well being and economic independence, concerns itself, for the most part, with those with hypertensive cardiovascular disease and with coronary artery disease.[1,2]

Hypertensive and Coronary Heart Disease: Hypertensive cardiovascular disease is very common. The disability may arise from the heart, the cerebral circulation or the kidneys. About 60 per cent of patients with hypertension die cardiac deaths. A high diastolic pressure in a middle aged person is an immediate threat to the heart; the working capacity of such a person should be evaluated as though he actually had heart disease.

Routinely, our prognosis is guarded for patients with angina pectoris or myocardial infarction. Many patients with coronary insufficiency, whether mild on unusual effort or severe at rest, improve spontaneously or may even recover completely. Such patients are well many years after the first attack, even though electrocardiograms continue to be abnormal. In coronary thrombosis with infarction, a well-healed scar may cause no trouble for the remainder of a long life.[3]

The signs and symptoms of diminished cardiac reserve depend on the interpretation of the patient's appraisal of any symptomatology resulting from his everyday activities. How far can he walk, on level ground, uphill, against the wind, how many flights of stairs can he climb without discomfort, what happens when he lifts or carries, twists the body, stoops, crouches, sits or stands for a long time, eats or dresses? Does he become short of breath? Do his feet or ankles swell? Does he suffer pain at rest or on exertion?

Other factors to be considered in estimating work capacity are the patient's emotional status, noncardiac disabling conditions, and his previous occupational activity. Having heart disease does not automatically enable your patient to sit down and play the piano; nor do you expect a person who had been doing light work to undertake strenuous work after an attack of coronary thrombosis. Previous recreational and athletic activities, not alone occupation, should be considered. One must also recognize the fact that our patient's chronologic age is not the same as his physical age. Another factor to consider is heredity. The prognosis in the case of a 40-year-old man with coronary thrombosis is necessarily worse if both parents died from the same disease when they were in their forties or fifties. Does it pay to retrain such an individual? Would it be better to have him find work, any work within his physical limitations?

Work Classification

The very nature of the factors discussed indicate that there is no simple formula, no

scale of points and measurements that can be applied, in estimating work capacity.[2] Only after one has evaluated his patient as an individual, can one state arbitrarily but specifically, just what he may do. It is best to adhere to simple terms, describing ordinary occupational and nonoccupational activities, such as crouching, standing, walking, climbing, lifting, in giving a prescription for work activity and in setting limitations. For example, you can have your patient eliminate lifting entirely from his daily routine, or you can permit him to lift up to ten pounds fifteen times a day, depending on the particular situation. You can permit him to walk ten to twenty blocks, or three blocks or less, depending upon the results of your study. But the recommendations made must be specific.

At the Work Classification Unit, the physician puts his recommendations on what is called a Work Classification Sheet. The sheet is returned to the referring agency with the specific recommendations. Those recommendations have been explained to the patient. The physical limitations and their cause have also been explained to him. The form itself is self-explanatory. A brief description of functional and therapeutic classification is printed on it so that such a classification can be understood by a lay person. If the referring agency is an employer, he usually intends to re-employ the patient in some capacity the unit has set. If the referring agency is a voluntary or a governmental agency, it tries to follow the suggestions in securing a proper job for the individual, or for retraining him, or even in getting necessary treatment for his noncardiac disabling factors.

The proof of the correctness of our real estimation of the patient's working capacity will be in the follow-up study and in the continued evaluation in the patient. Physical limitations can be increased or decreased, and morale can be maintained.

The actual work that the patient can perform, within the limitations one has set, depends again on other factors—the patient's background, education and training. Unless we know the patient and his capabilities extremely well, we cannot tell him what work he can do. One can merely specify and enumerate the extent of his physical activities. However, we can and should help the patient determine whether or not a particular job fits into the limitations we have set.

Job Description and Classification

You have been able to tell the patient whether or not he can return to his old job; whether or not he can accept another position. In giving such advice, do not rely on your knowledge and imagination of what a certain job title implies. The distinction between manager and foreman, between trade and manufacturing, and so on, is often hard to make. The Dictionary of Occupational Titles issued by the United States Department of Labor contains some 40,000 listings. The Federal Security Agency Industrial Code contains about 1,000 industries. In all cases, have the patient give an accurate description of what he did and what he intends to do. Such a description should, more or less, follow the standard forms used by personnel departments, and employment agencies.

A Job Description and Evaluation Form is used by many firms. There is a space for a job title, which is usually filled in with some plant colloquialism. The important feature is the actual word description of the job, the material and equipment used. The remainder of the form contains several headings and subdivisions requiring a notation and serving as an excellent check list. For example, under "Job Environment" the entries to be checked are: hot, cold, floor, bench, etc. Other headings are: physical requirements, mental requirements, skill, responsibility, safety of others. This latter is important. Eastman Kodak goes a step further by giving a definition for the various physical activities, and printing them directly on the form.[4] Some definitions are:

Lifting, raising or lowering an object from one level to another, by using the arms, legs and back muscles;

Walking, moving about on the feet by taking alternate steps;

Stooping, bending the body forward by flexing the spine at the waist.

The form gives about 25 definitions for common activities and provides space for listing others not defined. It makes it much easier to match a handicapped person, with well-defined limitations, into a properly described job. Vagueness could keep that man from employment or could keep a job from being filled.

One should always consider the means of travel to and from work, for that may account for the most strenuous exertion in the daily working routine. A recent issue of the *New York Times*[5] under a headline "Doctors Urge Ban on Cardiac Driver" quotes a member of the policy-making committee of the New York State Medical Society as saying: "New York has ignored the increasing highway accident potential created by insidious disease" and that Pennsylvania was seeking a formula to enable doctors to prevent patients with heart disease from driving cars. Such a procedure would certainly remove from industry many of the people we have been following at the Unit, for they have been working only because they can reach their places of employment by driving their own cars.

In following some sort of routine such as this, you can properly advise the patient whether a specific job can be done within his physical limitations, and so reserve the use of the limited, specialized technics of rehabilitation for unusually complicated cases, or as the last resort in getting the patient back to work.

But is it enough just to get your patient back to work and to observe him periodically? John Ruskin who may not have been an expert on rehabilitation but who certainly knew how to express himself, wrote: "In order that people may be happy in their work, these three things are needed: They must be fit for it. They must not do too much of it. And they must have a sense of success in it." You must help your patient re-evaluate his criteria of success. Getting back to work should in and of itself be considered success.

Summary

It can be extremely difficult to assess the work ability of a person suffering with heart disease. Each case must be appraised individually, since the many factors to be considered vary so greatly from case to case. Each factor must be verified, and a total evaluation must be determined. Recommendations to the patient must be specific even though arbitrary; ambiguity must be avoided.

The physical demands of a job, not a job title, must be carefully considered. The condition of the labor market also determines to a great extent whether or not the patient can return to work.

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The Function of Government and Industry in Rehabilitation of the Cardiac*

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WE ALL agree that many cardiacs can work. Our task is to discover and remove the impediments which keep the patient isolated, to analyze the contributions which each segment of society can make to help the seemingly disabled cardiac recover his potential industrial capabilities, and, ultimately, to restore him to profitable employment. To achieve these ends, physicians must be able to correlate a considerable mass of nonmedical information with their professional knowledge. They should be familiar with job requirements. They must know the needs of industry and labor. They must keep in mind the many laws which have been enacted to aid in rehabilitating the physically handicapped.

The rehabilitation problem would be simple, indeed, if only the application of a rule or law were required to solve it. People would then not have thought it important enough to devote considerable time, money, discussion and writing to the subject. It is apparent that the solution is difficult and requires the various experiences of many adequately trained persons. An accurate diagnosis, a study of the patient's surroundings, an analysis of his work history and his outlook, a consideration of his educational background, a knowledge of the available sources of re-education and an insight into other factors are essential for preparing the patient for work. All these are of little value, however, unless work can be obtained.

It is important to induce an employer to "buy" the services of the rehabilitated patient who has been thoroughly processed by his physician, by social workers, by workshops, work classification units and others. All our efforts are in vain if some work for gain cannot be found. Those interested in the problem do not question the wisdom of permitting persons with heart disease to obtain adequate employment, or of encouraging industry to hire them for suitable work. To make more work opportunities available for those so handicapped, industry has a right to look to government, labor, physicians and personnel experts for advice and guidance. Those who are trained to give this aid, should make it available to employers, who, in the final analysis, accept the responsibility for the employment of the partially disabled.

ROLE OF GOVERNMENT AND INDUSTRY

Function of Government: Government assumes an important place in our consideration and makes its contributions, too. Laws have been enacted which give relative protection to the employer who engages the handicapped without diminishing the legal protection afforded the employee; yet which do not lessen the employer's incentive to seek new methods for the prevention of accidents or occupational diseases.[1]

It is interesting to note that 43 states have some form of "Second Injury Law." However, the diseases covered and the legal restrictions vary from one political subdivision to another, so that comparison is extremely difficult. In the New York State Law, the presence of some degree of permanent disability rather than the medical diagnosis is the requisite for employing the handicapped. It has been thought that it

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was dangerous to hire certain handicapped persons, at least from the compensation point of view. The law, however, has attempted to reduce the employer's responsibility for compensation, when the physically handicapped are injured in the course of further employment.

Function of Industry: This legal inducement to engage disabled workers must be clearly understood by industry. Every effort should be made to acquaint the potential employer and employee with the Second Injury Law.[1] Employers who know the relative protection which the law affords them, may manifest a greater willingness to engage the experienced handicapped worker, and thereby reduce or avoid costly labor turnover.

Industry may then plan a program, setting aside a certain portion of its work for these people. Industrial concerns which employ a large number of workers usually have experienced lay personnel and specially trained physicians, who can make accurate job analyses and suggest proper work placement for each partially disabled individual. Most plants in our country however, employ fewer than 100 people, and necessarily must look to the local physician for this advice and guidance. It is, therefore, essential that the local physician, as well as industrial physicians, have a sound knowledge of job analysis and selective placement and be fully familiar with the sources of this information.

Selective placement is based on knowledge of the particular job and the potential employee. Both must be thoroughly studied—the balance resulting in the placement. The foreman, personnel director, and the physician, together, must make the assignment with the full understanding that no change in the type and degree of work will be made without a conference. The improper application of a well conceived plan of selective placement may result in such poor experience, that the employer may discontinue hiring the disabled, thereby closing off future opportunities for others. The follow-up mechanism must be clearly stated and there must be strict adherence to it.

It has been shown that the work records of this special group of handicapped employees are good. Though they had heretofore been considered unemployable, their work is not only a boon to society, through the services they render, but is also of inestimable value to themselves.

One of the newspapers discussed this subject in its editorial and stated in part:[2]

". . . . . The National Association of Manufacturers, after a study of the situation, testifies for the usefulness of the disabled. So do the business firms large and small that hire them—and hired some sixty thousand last year alone. It has been proved that the handicapped worker is equal to, and is sometimes better than, his able-bodied brother in such important areas as attendance, turnover, safety and productivity. The business firm that turns away an applicant for employment simply because he is physically handicapped is acting not only against the public good but also against its own best interests."

Second Injury Law: The Legislature of New York State has for some time been aware of the problems with which the employment of previously disabled workers is fraught. It has made clear its intent to help solve the problem, by the wording of the introduction to the Second Injury Law (Section 15-8 of the New York State Workmen's Compensation Law).

The employer is thereby relieved of considerable responsibility for compensation, when he hires a permanently partially disabled person who subsequently has an increased permanent disability as a result of his work. The proper application of the legal requisites prescribed is essential for obtaining the benefits which the Law offers.

Conclusion

It is hoped the physician will have a clearer understanding of his important role in rehabilitating the disabled cardiac, that industry will become more aware of the benefits to be derived from a plan of hiring handicapped people, that its policies and practices in this regard will be based on knowledge, and that these together will serve to stimulate still further the employment of permanently partially disabled men and women.

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The Insatiable Heart

A Lawyer's Viewpoint of Compensation Problems of the Cardiac*

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THE PROBLEMS involved in providing workmen's compensation payments for employees who suffer disability or death as a result of heart disease are manifold and multiplying. In the opinion of many knowledgeable observers, the problems are rapidly building to a crisis situation. An explosion is inevitable unless the trend of recent developments in this area can be arrested and actually reversed.

Until the phenomenon of Aggravation appeared on the medico-legal scene, defense of workmen's compensation claims was deemed a routine chore. It was regarded and often treated as a clerical function. Competition naturally developed among managements clearly dedicated to saving industry tangible dollars in claims handling costs.

Viewing the nation's amazing business, commercial and manufacturing growth, the insurance industry lost little time in proving itself equal to the task of furnishing needed coverages never before envisioned. But while weaving this vital and ever-spreading blanket of protective coverage, claims management found itself faced with increasingly inadequate manpower pools. It found available too few young men and women to fill its increasing personnel needs.

Into this situation of business expansion and paper-thin spreading of available talent there came an unheralded visitor. He was not entirely unwanted—he accomplished the righting of some grave injustices which had been wrought by inadequate medical awareness of the incidental but catastrophic effect of an untoward outside influence on latent, or even patent, lesions whose etiology was known to be non-occupational.

This visitor, however, was quickly embraced by those administrators whose trusted position as judge and jury is twisted beyond recognition by their belief that votes accrue in equal ratio to the size of compensation awards handed out indiscriminately. Our visitor was welcomed warmly also by segments of the medical profession whose medical concepts have become web-like, chameleon-like and increasingly sensitive to the monetary rewards which easy medical conscience can yield. Our visitor received an equally warm welcome from groups within the legal profession who parlayed these facets into a most lucrative, specialized practice and naturally encouraged and abetted the further development of this beneficent climate.

Aggravation was our visitor and he came accompanied by his kin: Activation and Acceleration.

CONSEQUENCES OF THE CONCEPT OF AGGRAVATION

In a claims environment where cause and effect were only occasionally disputed and, in such cases, quickly resolved on definitive standards and evidence, the entry of these three A's proved well-nigh catastrophic. Every biologic and pathologic change of hypertensive, rheumatic, congenital, and arteriosclerotic heart disease suddenly became a charge upon industrial society, and its insurance stand-in, which

* Read at the Legal Conference of the Industrial Hygiene Foundation at the Mellon Institute in Pittsburgh, Pennsylvania, October 30, 1957.

first displayed annoyance; then indignation; now—alarm.

The annoyance phase was characterized by an attempt to temper the situation through amicable disposition. The amicability was short-lived. The indignation phase followed quickly, spurred by increasingly avid demands for benefits in seemingly invalid claims, and eventual demands—no longer for a slice, but for the whole cake. Contests resulted. From them came compensation rule by the Courts, with legal decisions assuming dominion. These decisions created Compensation-Law-by-Court-Decision—and eventually some jurisdictions began accepting normal every-day job exertion as an aggravating factor in the presence of either known or unrecognized disease.

This indignation phase witnessed growing concern among those entrusted with the keeping of this segment of society's purse. It also witnessed great praise heaped upon the judiciary by those who were partaking of the seemingly unending warmth of compensation currency. During this era of rising concern accompanied by a shattering of complacency on the part of industry—during this era of Uriah Heep homage to Law-by-Decision—several important factors escaped notice:

The dearth of knowledgeable claims talent.

The poor and ineffectual defense handling from investigation, claims and legal levels where people took on the defeatist air of those constantly "wrong," pondering covetously the various occupations the members of which appear to be equally normal and who *do* seem to decide correctly.

The growing "nice-guyism" within a medical profession tending, more and more, to allow unsubstantiated and cobwebby medical testimony to go but weakly challenged.

Based on poor and, quite often, insufficient records, indignant appeals were taken—without benefit of cooler, less biased, less prejudiced, less emotionally-involved review. Appeals Courts accept what they find. They will not intrude into an assembled record. They find compensation laws that often do not define an industrial accident. In these jurisdictions, the Courts *will*—and *must*—define what an accident is in each case and in each case, separately, based on its own ill-advised and badly-drawn appeal record. Thus, from the natural phenomena of ulceration or hemorrhage of a degenerating arteriosclerotic artery in the heart, the brain or the leg—mostly the heart—has evolved the Law of the Industrial Handout.

In the midst of the indignation phase, rehabilitation of the compensable cardiac became confused with attempts for a monetary settlement. In its midst, reputable physicians began to "choose sides" and impartial medical panels became a bonanza one day and a calamity the next. In its midst, the gray became lost in the definitive search for that which is white or that which is black.

Much like the endocrine reaction Dr. Hans Selye is striving to bring into public awareness, industry and responsible unionism have had their Alarm Reaction. We are now in this Alarm Phase. How can a brake be placed on the insatiable heart? How can we avoid an era of employing only those without a scintilla of clinical or laboratory evidence of arterial disease? How can we equate reason, conscience and good medicine with sound administration of workmen's compensation laws?

In essence, how can we be reasonably certain to arrive at equitable decisions compensating only that portion for which industry should be responsible out of the big-as-life picture of artery disability?

Results of Study of Compensability

The Alarm Phase has resulted in scattered but numerous seminars and hundreds of papers, each advocating some correction or modification of existing approaches. Medically, these seminars discuss the pathologic and scientific rarity of a truly compensable coronary incident. Physicians are warned on the inescapable consequences to society of hasty diagnostic decisions; of the need for Criteria. Legally, we look with dismay and, too often, with defeatism, on the increasing volumes of decisional law that serve to nullify reasonable efforts to defend.

Industrially, by Association action we seek to modify malpractice of conscience, medicine, law, and administration via amendments to the law of each separate jurisdiction. In labor un-

ions, the far-sighted seek to deter this increasingly encroaching tide by pointing to the flow of industry to areas where the administration of compensation laws is not based on the mistaken notion that loose housekeeping of society's resources equals continuance in political power.

The work of these groups has resulted in interesting studies and suggested remedies. We are directed to the Nebraska Plan; the Utah Plan; various studies of union and employer groups. We are indebted to university studies such as those presently undertaken by Stanford University as well as to the continuing study by the Moreland Commission in New York. We look forward with interest to the study to be conducted by Cornell University in cooperation with the New York Workmen's Compensation Board at a contemplated cost of $135,000.

But there is no one solution to the problem. No one group alone can achieve significant, timely and lasting improvement of a situation portending an economic pitfall. To those who plead that medical criteria can be the solution, we submit that this would be important as an aid, but not as an answer. Criteria thus far established are definitive in areas which are clearly black or white. In the vast gray area of Aggravation, available criteria may only, and at best, be a guide.

Our office recently completed a study of 255 heart cases. Our findings are helpful and vividly illustrative of many facets of the problem. Of these 255 cases reviewed, 240 cases, or over 96 per cent, were based on claim of aggravation, activation, or acceleration of underlying coronary disease. Only 15 cases were found by us to be either black or white; and, on that basis, reasonably subject to available and recognized criteria.

In order that we might not be led astray by the forest in our own back yard, we asked corresponding law firms in eight other states to review their respective claims in similar vein. The results, when computed, showed a total grouping of 847 cases, of which 49 could be subjected to evaluation by recognized criteria. By this grouping, our own 96 per cent relegated to the gray limbo of medical and factual contest was lowered to 94 per cent.

It is to this gray area that the American College of Cardiology at its May meeting in Washington, D. C., determined to extend its inquiry. Its approach is nation-wide; its interest is the maintenance of the dignity, professional skill and honor of the cardiologic branch of the medical profession. Every reasonable aid should be extended to this organization in the furtherance of its study.

Recommendations for Determining Compensability in Cardiac Diseases

While we seek more definitive and universally acceptable criteria, we must simultaneously demand the formation of truly impartial panels of medical specialists whose very position in their medical community will achieve a review of a physician's testimony by his medical peers without divesting the administrative agency of its quasi-judicial power of decision. Different population figures necessitate varied approaches to the method of selection of these panels. Patient exploration and agreement on the avenues for their selection by both labor and management will obviate much of the pseudo-medical crystal-ball gazing that occupies so much of our high courts attention and memoranda of decision.

With the development of criteria believed reasonable by reasonable men, we should support equally reasonable amendments to our existing compensation statutes. Each jurisdiction has developed a law servicing its geographic, population, and occupational needs. The laws of such states warrant amendment calculated to establish compensation benefit for that portion of a disability which within reasonable certainty and reasonable criteria was occasioned by the outside and untoward effect of industrial accident. It is this most important need of apportionment of that which is accident-imposed, and that which is purely the result of a degenerative underlying disease, that criteria, truly impartial medical panels, and statutory law can meet.

While our attention is devoted to these goals, our day-to-day tasks must be faced. We cannot indulge in annoyance or indignation, no matter how righteous. If we do, we must accompany

these emotional escape-valves with a determination that every claim of this nature will be thoroughly and expertly investigated; that every aspect of past and present activity other than occupation, will be inquired into; that competent medical examinations will be secured; that the medical specialist selected shall have the benefit of all of our knowledge of the claim and any hospital files available; that on such proper basis legitimate claims will be paid. Of equal necessity is that they be followed up to insure the best possible medical regimen, with encouragement to return to social and economic activity, in short, true rehabilitation. In a situation of reasonable doubt, defense must not be a half-hearted resort to the defeatist-minded who subscribe to the doctrine of too little investigation, too late, but to those who will inject their own thinking and experience into exploration of all avenues of lay and medical inquiry to the end that the completed record is not wishful thinking.

Only by the grouping of these segments; only by the realistic awareness that every professional and every individual effort is involved and necessary; only by the conscience that should guide labor-management relations—by these only, and by these in combination, will the Alarm Phase of the cardiac problem be satisfactorily resolved.

Clinical Studies

Intracardiac Phonocardiography in Mitral and Aortic Valve Lesions*

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Chicago, Illinois

Intracardiac phonocardiography (i.c. phono) is a recently described technic. Right heart i.c. phono was independently described by Soulié,[1] Yamakawa *et al.*,[2] Lewis *et al.*,[3] and Moscovitz *et al.*[4] Left heart i.c. phono was described by Luisada and Liu[5,6] by using an entirely different principle which can be applied to either side of the heart.

The present study is an investigation of the possible applications of i.c. phono in 15 rheumatic patients with mitral and aortic defects and in two subjects without valvular lesions.

Technic

The 17 clinical cases which were studied were submitted to left heart catheterization according to the method of Björk[7] with the modifications of Kent *et al.*[8] and Fisher *et al.*[9] The patients were in a prone position over a fluoroscopic table and a needle was introduced into the left atrium from the right of the spine. Pressure tracings were recorded with a Statham P 23 D strain gauge. The recording apparatus was a 6 channel universal cardiograph with cathode-ray oscilloscopes built by Electronics for Medicine.

Intracardiac phonocardiograms were recorded, according to previous descriptions,[5,6] by connecting the strain gauge channel, by means of a short cable, to the phono channel. The medium and high frequency vibrations of the gauge were differentiated, amplified, and filtered, then recorded by the phono channel. This system allows one to register the vibrations of the blood within the various chambers with-

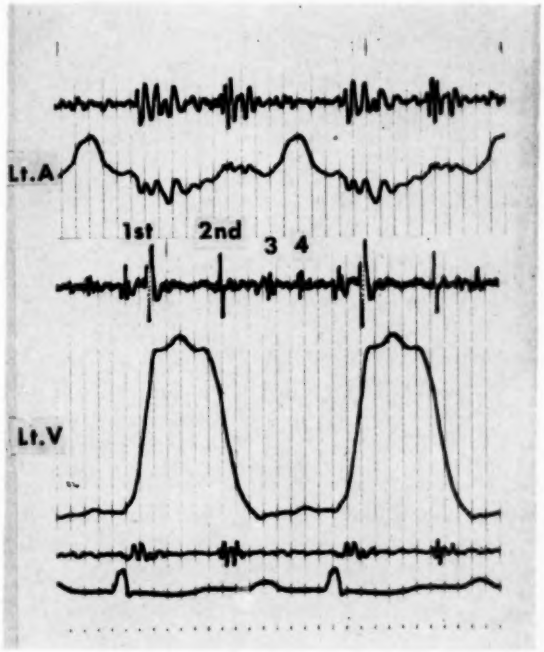

Fig. 1. Left atrial (above) and left ventricular (below) pressure tracings in a subject with normal mitral valve. The phonocardiograms superimposed over the pressure tracings are intracardiac phonocardiograms from the same chambers. At the bottom: external phonocardiogram and electrocardiogram.

* From the Division of Cardiology of The Chicago Medical School at Mount Sinai Hospital.

This study was made under the tenure of a Teaching Grant of the National Heart Institute, U.S.P.H.S., and with the help of Research Grants of the National Heart Institute (H-3416) and the Chicago Heart Association.

out introducing any additional device into the heart. Registration can be made from the needle (left atrium) or from a thin polyethylene catheter (left atrium, left ventricle, aorta). The polyethylene catheter is used for left ventricular catheterization and for retrograde aortic catheterization (following puncture of the brachial artery with a $1^1/_2$ inch long 18-gauge thin-walled needle).

The pressure tracings were recorded at that degree of amplification which was most suitable for obtaining a satisfactory tracing. The intracardiac phonocardiogram was recorded in the bands 60-110, 60-250, or 60-500. Occasionally, the band 30-110 was also used. It should be noted that the degree of attenuation of the filters is gradual,* so that higher and lower pitched vibrations were still recorded, though minimized.

Among the 17 cases, the study of pressure gradients and that of pressure patterns led to the following dynamic diagnoses:

Normal valves = 2
Severe mitral stenosis (mitral insufficiency minimal or absent) = 3
Mitral stenosis and insufficiency = 7 (one case, also aortic lesion).
Severe mitral insufficiency (mitral stenosis minimal or absent) = 3
Aortic stenosis and insufficiency = 2

Results

(1) Subjects with normal valves

Two patients presenting no murmurs were submitted to both right and left catheterization. The pressure tracings revealed no valvular lesions.

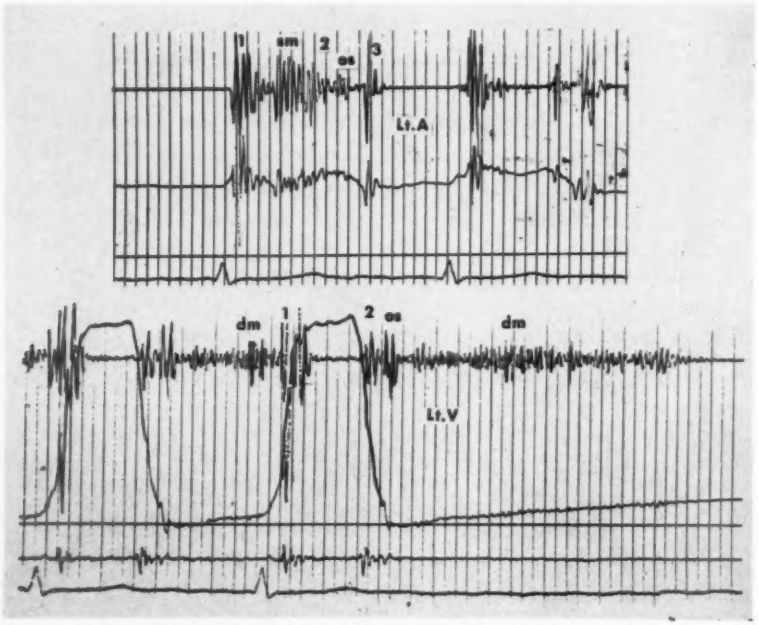

Fig. 2. Left atrial tracings (above) and left ventricular tracings (below) in a case of pure mitral stenosis (minimal regurgitation). In each film, from above: i.c. phono, pressure, external phono, ECG. There is a large opening snap (OS) in both the atrium and the ventricle. In the latter, it is followed by a rumbling diastolic murmur (dm).

Left Ventricular Phono: The intracardiac heart sound tracing recorded in the left ventricle of subject 1 reveals two components within *the first heart sound* (Fig. 1). The first component having two to three vibrations, is smaller and corresponds to the beginning of the rise of left ventricular pressure; it coincides with the closure of the mitral valve and follows the Q wave by 0.035 sec. The second, larger component, having two vibrations, occurs at $^2/_3$ of the rise of the ventricular pressure and seems to coincide

* The filters decreased the signals at a rate of 12 decibels per octave respectively above and below the selected frequencies.

with the opening of the aortic valve; it follows the Q wave by 0.105 sec. *The second heart sound*, presenting a single vibration, coincides with the first, larger vibration of the 2nd sound, recorded over the midprecordium (aortic component). It is, therefore, due to closure of the aortic valve.

Left Atrial Phono: The intracardiac sound tracing recorded in the left atrium of the same subject reveals a group of vibrations of *the first sound* which coincides with the second group re-

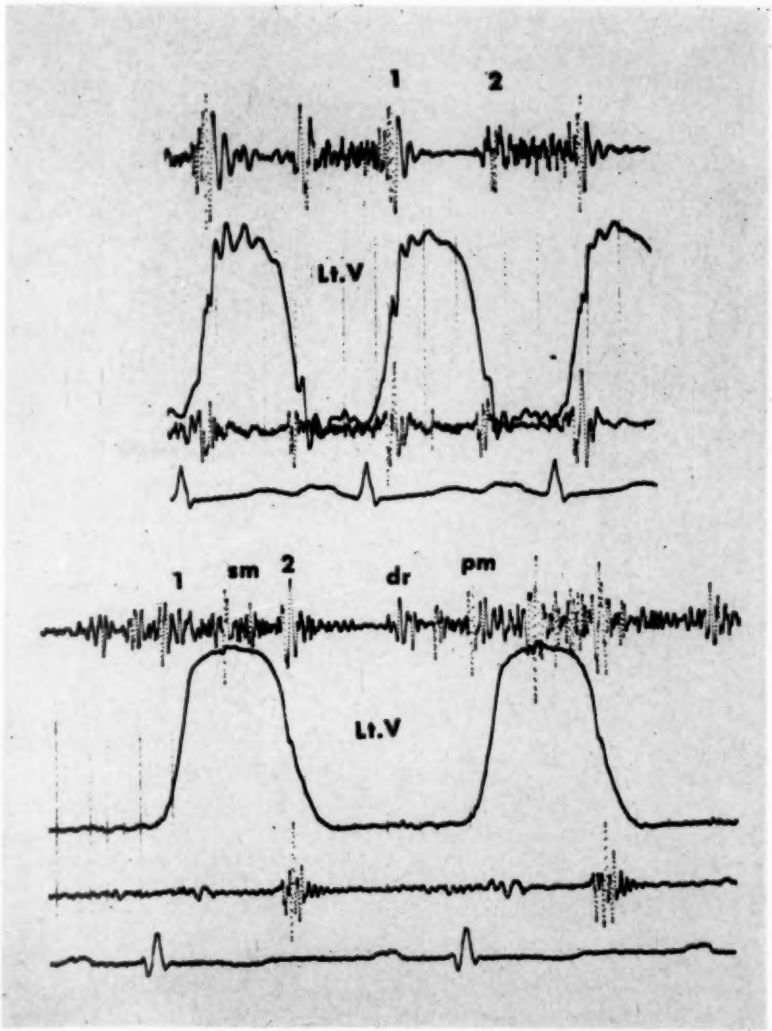

Fig. 3. Left ventricular tracings in two cases of pure mitral stenosis and normal sinus rhythm. In each film, from above: i.c. phono, pressure, external phono, ECG. Diastolic rumble (dr) and presystolic murmur (pm) are present in both cases.

There is no murmur but a few minimal vibrations can be observed during systole. *The third heart sound*, presenting one or two vibrations, occurs 0.13 to 0.14 sec after the second sound, in coincidence with the rapid filling of the left ventricle. *The fourth heart sound*, presenting a triphasic vibration, coincides with left atrial contraction.

corded in the left ventricle (aortic component of the 1st sound). The *second sound*, presenting a triphasic vibration, coincides with the aortic component of the second sound, recorded in the left ventricle. The *opening sound of the mitral valve* presents a triphasic vibration and follows

the first vibration of the second sound by 0.06 sec; it coincides with the V wave of the left atrial pressure tracing. After the mitral opening sound, the remaining diastole is clear, except for a few low frequency vibrations coinciding with the atrial contraction; these vibrations may be termed "fourth heart sound" because they coincide with a larger, more rapid, and more distinct sound occurring within the ventricular cavity (Fig. 1).

(2) SEVERE MITRAL STENOSIS (MITRAL INSUFFICIENCY MINIMAL OR ABSENT)

Tracings recorded in the left atrium revealed *no* systolic murmur in two cases and a few, low frequency, systolic vibrations in decrescendo in one case. A third case had *an opening snap of the mitral valve.* Tracings recorded in the left ventricle of one case (Fig. 2) also revealed an opening snap of the mitral valve, the largest vibration of which followed the aortic compo-

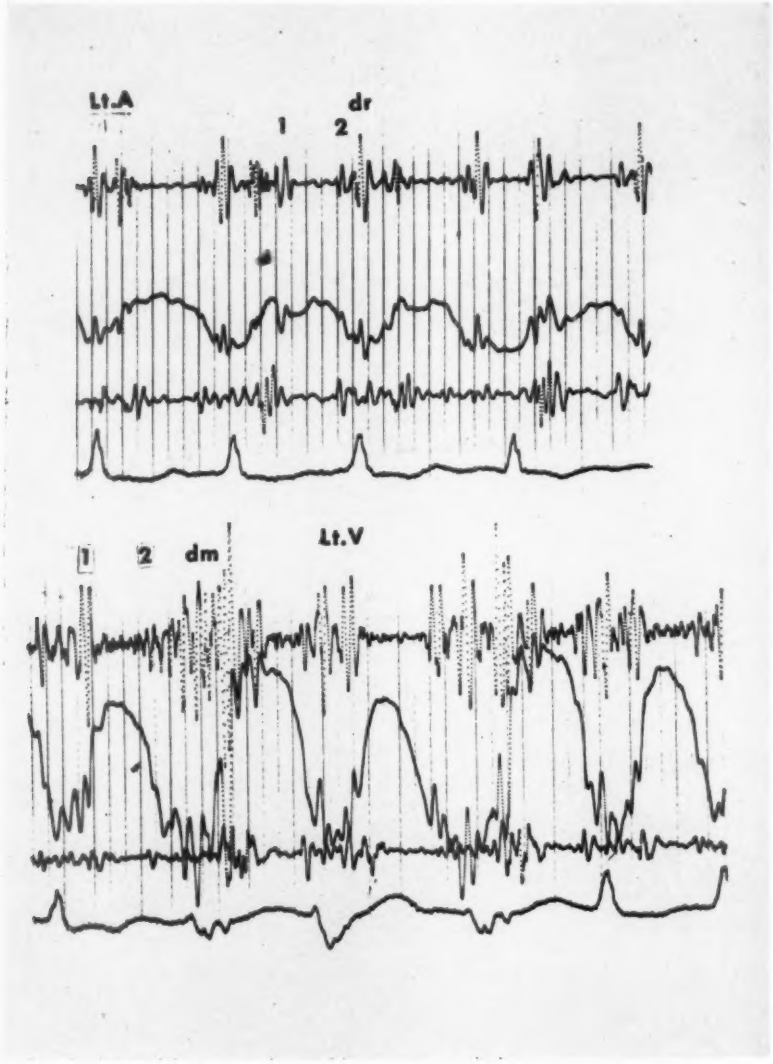

Fig. 4. Mitral stenosis (predominant) and insufficiency. Left atrial tracings are above and left ventricular tracings below. Atrium—delayed 1st sound, short diastolic rumble (dr); no systolic murmur; systolic plateau in the pressure curve. Ventricle—large diastolic murmur (dm).

nent of the 2nd sound by 0.05 sec. Following this snap, a *diastolic rumble with presystolic accentuation* was clearly visible. The largest vibration of the 1st sound followed the Q wave by 0.075 to 0.080 sec. In another case, the left ventricular tracing revealed the following data: in the band 15-250, a prolonged opening snap and a 3rd sound; in the bands 30-250 and 60-500 (slight pullback), a prolonged all-diastolic rumble (Fig. 3).

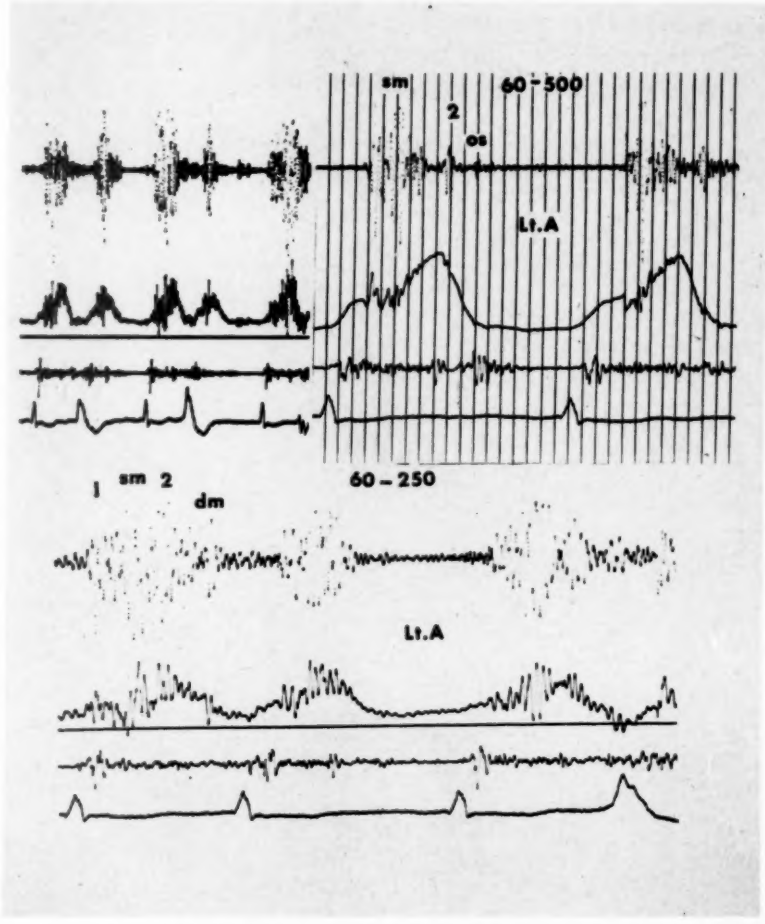

Fig. 5. Left atrial tracings in pure mitral insufficiency. Upper left—low speed. Upper right, catheter in center of chamber. Lower tracings—catheter near the valve. At a distance from the valve, there is a late systolic pressure wave and a short, early systolic murmur. Near the valve, the pressure tracing reveals the systolic thrill and the sound tracing shows a longer systolic murmur.

(3) MITRAL STENOSIS AND INSUFFICIENCY

(*a*) *Left Ventricle:* The left ventricular tracings revealed abnormalities which were similar to those described for pure stenosis. One case had atrial fibrillation and showed a gradually fading *diastolic murmur* whenever diastole was prolonged. In the cycle which followed a short diastole, the diastolic murmur was larger and more prolonged.

(*b*) *Left Atrium:* The left atrial tracings revealed an *opening snap* of the mitral valve in four cases out of seven. They also revealed the vibrations of a *systolic murmur* in five out of seven cases (see below). This murmur was larger after a longer diastole and, at times, absent after a short one (Fig. 4). Diastolic vibrations were recorded in one case.

(4) MITRAL INSUFFICIENCY (MITRAL STENOSIS MINIMAL OR ABSENT)

(*a*) *Left Ventricle:* The ventricle was not entered in one case. In the other two cases, a systolic murmur was recorded. In one, a short and small *diastolic rumble* was recorded.

(*b*) *Left Atrium:* The left atrium of these three cases (as well as that of seven cases with mitral insufficiency and stenosis) revealed the vibrations of a *systolic murmur*. This was usually shorter and of smaller amplitude after a short diastole. It was better recorded through the catheter than through the needle and became particularly large when the tip of the catheter approached the mitral valve (Fig. 5).

In one case of combined valvular lesions, where the phonocardiogram revealed an apical systolic murmur and the left atrial pressure tracing revealed only a minimal systolic elevation, the i.c. phono of the left atrium showed large vibrations in late systole coinciding with a *thrill* in the pressure tracing. It was interpreted as due to minimal insufficiency.

(5) AORTIC STENOSIS AND INSUFFICIENCY

Aorta: The tracings recorded in the ascending aorta chiefly revealed *the systolic murmur* (Fig. 6). *A diastolic murmur* was also apparent in cases with severe insufficiency while it was nonexistent in the others (Fig. 7 and 8).

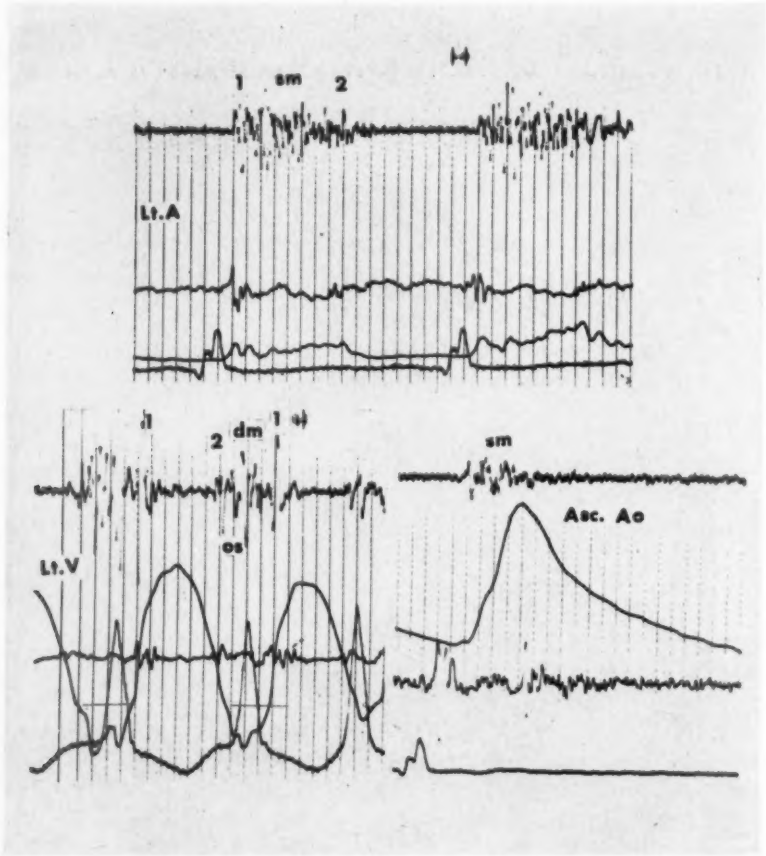

Fig. 6. Left atrial, left ventricular, and aortic tracings in a patient with mitral stenosis (moderate), mitral insufficiency (minimal) and aortic insufficiency. Probable minimal aortic stenosis. The left atrial systolic murmur does not correspond to a systolic elevation of pressure and is, therefore, evidence of a minimal regurgitation, dynamically insignificant.

The ventricular and atrial tracings revealed the data pertinent to mitral lesions if they were present, with the exception of a *functional diastolic rumble* in the left ventricle recorded in one case.

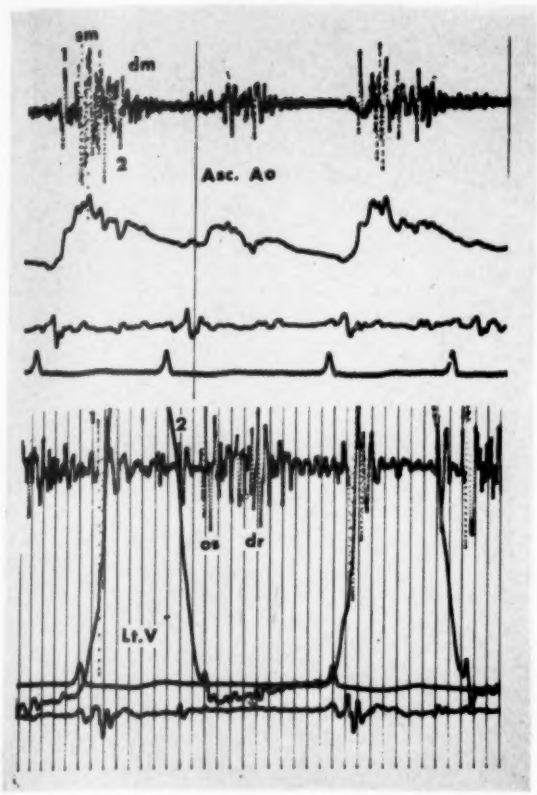

Fig. 7. Aortic and left ventricular tracings in a patient with aortic stenosis (moderate) and insufficiency (minimal) and mitral stenosis (severe). Diamond-shaped systolic murmur and minimal diastolic murmur within the aorta. Large diastolic rumble and opening snap within the left ventricle.

A patient with aortic stenosis and insufficiency and *no* gradient across the mitral valve presented a large but late diastolic murmur within the left ventricle. This was interperted as due to eddies in the left ventricular chamber (relative stenosis—Austin Flint murmur).

Discussion

In the 17 cases reported here, the hemodynamic diagnosis was based on the details of the pressure pattern of the left atrium (Luisada and Liu), as well as on the study of pressure gradients (Björk, Fisher, Wood). The external phonocardiogram and the various clinical, roentgenologic, and electrocardiographic data were often in agreement with those of catheterization while, in some cases, there was some discrepancy. In certain cases, the diagnosis of mitral insufficiency and stenosis was entertained. The finding of a large systolic murmur in the left atrium confirmed and increased the value of catheterization data (systolic elevation of pressure). If, on the other hand, the pressure pattern was normal and a systolic murmur was found only in the vicinity of the mitral valve, this was accepted as evidence of minimal (dynamically insignificant) mitral insufficiency. If the systolic murmur was present only in the ventricle, then a different mechanism was

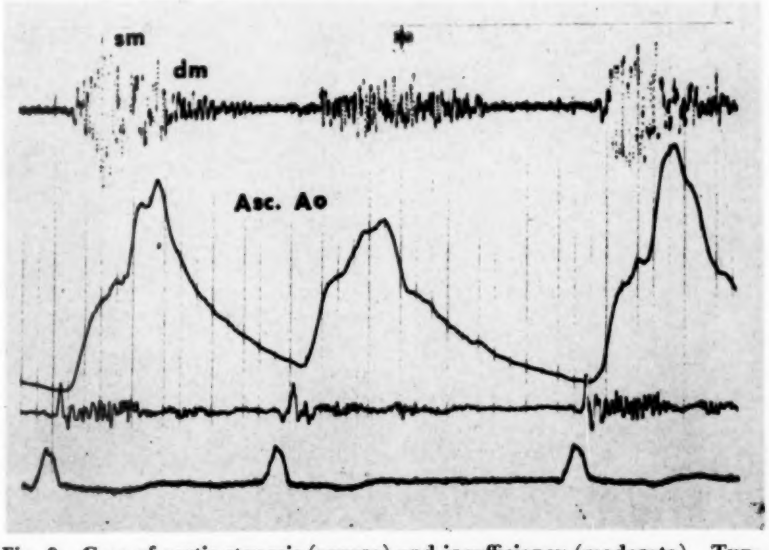

Fig. 8. Case of aortic stenosis (severe) and insufficiency (moderate). Typical pulse curve and diamond-shaped murmur within aorta.

postulated (functional mechanism). If it was only or mainly in the aorta, aortic stenosis (absolute or relative) was recognized as the cause.

The finding of a large diastolic rumble in the left ventricle was usually evidence of mitral stenosis. However, an exceptional case was observed where the pressure gradient across the mitral valve was normal. In this case, as there was aortic insufficiency, the diastolic murmur was considered an Austin Flint murmur. However, in other cases, the possibility of a minimal, dynamically insignificant stenosis should be considered.

Timing of the heart sounds and their valvular components was found accurate. The vibrations of *the first sound* within the left ventricle reflect the closure of the mitral valve and then the opening of the aortic valve. The vibrations of *the second sound* within the left ventricle reflect the closure of the aortic valve. An *opening snap* of the mitral valve was recorded within the left ventricle (and occasionally also within the left atrium) in patients with lesions of the mitral valve. On the other hand, smaller vibrations may be observed: (a) at the time of opening of the mitral valve (opening sound) (atrium or ventricle); (b) at the time of atrial contraction (atrium); (c) at the time of rapid filling (ventricle). These are physiologic vibrations and do not indicate a lesion of the mitral valve (Fig. 1).

In three cases with ventricular arrhythmia, it was noted that a short diastole was followed by a smaller systolic murmur in the atrium and a larger diastolic murmur in the ventricle. This indicates that the murmurs were "flow murmurs" and were affected by the amount of blood existing in the chamber from which started the motion of the blood causing the murmur (smaller systolic murmur because of lesser ventricular filling; larger diastolic murmur because of engorgement of the atrium). This phenomenon was particularly evident in the case of the systolic murmur. Whenever a very early contraction caused an extreme abbreviation of diastole, the systolic murmur disappeared.

At the present stage of our study, we consider that the importance of the various methods in left heart catheterization is as follows:

(a) Pressure gradients (stenosis)
(b) Pressure patterns (insufficiency)
(c) Sound vibrations (stenosis or insufficiency)

The third method is still being investigated and a complete evaluation will be possible only on the basis of a large number of cases.

Intracardiac phonocardiography is barely beginning to yield results. This report is the first study of clinical intracardiac phonocardiography within the left heart. It is too early for a complete evaluation of the possible diagnostic advantages which this method may have in comparison with others, as only an extensive study and a continuous comparison with other existing methods can lead to definite conclusions.

Summary

Intracardiac phonocardiograms were studied during left heart catheterization in two normal subjects and 15 patients with mitral or aortic valve lesions.

Data pertaining to normal intracardiac, left atrial and left ventricular sounds are discussed.

Data obtained in mitral stenosis, mitral insufficiency, aortic stenosis and aortic insufficiency are reported.

The murmurs were best recorded in those chambers which received the blood flow (normal or pathologic) during the production of each murmur.

Observations dealing with the third or fourth heart sound and with the mitral opening snap are reported.

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Cardiovascular Problems in the United States Air Force*

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THE Air Force has many cardiovascular problems, especially those associated with high altitude flying and stresses produced in supersonic aircraft. In this presentation, however, I will touch upon several problem areas in the United States Air Force which are germane to the civilian practice of cardiology.

CORONARY DISEASE

The first problem occurs in the general area of ischemic or coronary heart disease. Statistical analysis of figures available for 1955 Air Force experience reveals that the incidence of arteriosclerotic heart disease among Air Force personnel is significantly lower than that observed in the civilian population for persons under age 40. For ages 40 and above, there is no evidence that Air Force experience is any different from that in the civilian population. As in the civilian population, the incidence rate of arteriosclerotic heart disease among Air Force personnel increases with age. The points are brought out in the tables herein published. (Tables I and II).

With the recent re-emphasis on dietary prophylaxis[3] and treatment[4] of ischemic heart disease, we have been asked about our plans for controlling the fat intake of Air Force personnel. The calculated daily fat content of the master menu contains an average of 198 g, about 1,800 calories out of a total of 4,000 calories estimated. The fat calories represent 45 per cent of the total menu. Two factors that remain unknown are the actual amount of fat consumed and the amount of supplements taken in the form of milk shakes, ice cream, candy, etc. This gave the Office of the Surgeon General grounds for concern and led us to refer the problem of fat intake to the National Research Council about a

TABLE I[1]

Incidence of Arteriosclerotic Heart Disease—Civilian Population 1950–54 (Four Years)

Framingham males			
Age	Population	New cases	Rate per year per 1,000
30–34	333	3	2.3
35–39	388	5	3.2
40–44	357	5	3.5
45–49	308	8	6.5
50–54	301	15	12.5
55 and Over	289	29	25.1

TABLE II[2]

Incidence of Arteriosclerotic Heart Disease—Military Population 1955 (One Year)

Air force males			
Age	Population	New cases*	Rate per year per 1,000
30–34	9,368	4	.4
35–39	8,063	10	1.2
40–44	2,570	13	5.1
45–49	907	5	5.5
50–54	231	3	13.0
55 and Over	92	4	43.6

* Number of cases in a random 10 per cent sample of Air Force personnel.

* Presented May 17, 1957 at the Annual Meeting of the American College of Cardiology, Washington, D. C.

year ago. The question was considered specifically by the National Academy of Sciences—National Research Council's Food and Nutrition Board last October.[5] "They made no specific recommendation on the subject as they felt that there was not enough real data available to justify such a statement." We are satisfied to maintain the status quo in respect to the master menu since most of the evidence incriminating dietary fat is correlative[6] rather than experimental.

As a matter of interest, the Air Force has been carrying on since 1953 longitudinal blood lipid studies, inclusive of lipoproteins determined by the ultracentrifuge technic, on a group of approximately 150 military and civilian executives belonging to the Air Force establishment. This program is still underway and should ultimately prove revealing.

Rheumatic Fever

In view of recent publicity[7,8] given to the control of streptococcal sore throat and its sequelae, it would appear that this second problem would be fairly well controlled. However, our statistics do not show the decrease which was to be expected. Table III gives the incidence of streptococcal sore throat and rheumatic fever from 1951 through 1956.

TABLE III*

Reported Incidence/100,000 Strength

Year*	1951	1952	1953	1954	1955	1956
Streptococcal sore throat	780	572	661	631	860	837
Rheumatic fever (with and without heart involvement)	46	66	55	35	65	44

* For 1951–55, figures are based on all admissions from a 10 per cent sample of the Air Force. For 1956, figures are derived from a summary reporting of the entire Air Force.

The apparent high ratio of rheumatic fever to streptococcal disease can be explained by a probable underreporting of streptococcal disease since in the military service specific diagnostic information is available only from inpatient reports, not from cases treated on an outpatient basis. In addition, some inpatients who actually may have streptococcal disease are not so diagnosed and therefore recorded as having "other acute respiratory disease."

New enlistments occur at a rate of approximately 15 per cent a year, thereby providing a suitable seed bed for the propagation of streptococcal disease.

The basic military training and reception centers have decreased from three to one in number. After several weeks, the recruit is sent to one of seven technical training bases. The bulk of streptococcal sore throat and rheumatic fever occurs in several bases, which hold the recruit population, north of the 38th parallel.

We intend to pursue this subject further with the dual approach of studying the possibility of mass prophylaxis, as indicated, with large doses of benzathine penicillin G at our single reception center, where 75 per cent of the recruits are moved out in four weeks, and of better bacteriologic identification of beta hemolytic streptococcus from cultures of the nasopharynx at Air Force bases. The so-called classic appearance of the streptococcal throat has been described, but we and others[8] have isolated, in face of known streptococcal outbreaks, hemolytic streptococci from throats having the appearance of a viral infection.

Electrocardiographic Screening

The third problem has to do primarily with the use of the electrocardiogram as a screening device for the detection of heart disease. Since 1940,[9] the need for base line electrocardiograms on flying personnel has been recognized. As a result of the Royal Canadian Air Force experience[10] it can be expected that the electrocardiograms will reveal 5.4 per 1,000 to have heart disease unrecognized by previous routine examinations.

Since World War II, the Air Force has required an annual physical evaluation of its flying personnel. In January 1953, as part of the Air Force executive type of annual medical evaluation, the taking of an electrocardiogram beginning at age 40 was made mandatory. (Several of the major air commands are already doing electrocardiograms on an annual basis for

all their officer flying personnel.) Then three types of electrocardiographic defects began to trouble the Air Crew Standards Branch. They are the complete right bundle branch block, Wolff-Parkinson-White pattern and T wave changes.

In July 1956, detailed electrocardiographic deviations were described which would be considered not acceptable for initial selection into flying training. Likewise, similar criteria were agreed upon for removal from flying status. This latter group is reviewed by the Air Crew Standards Branch, Physical Standards Division, Office of the Surgeon General. Advisory service is provided by the Consultant in Internal Medicine.

On April 4, 1957, a directive requiring the creation of a central USAF electrocardiographic record repository was published. Within twelve months, base-line tracings will be taken on all officers on flying status below the age of 40. Electrocardiograms will also be taken on all selectees for flying training. They are already required for all cadets entering the USAF Academy. These reference tracings will be filed at the Air Force School of Aviation Medicine. In addition, copies of electrocardiograms of flying personnel taken as part of their annual evaluation and of those taken for any other reason, e.g., hospitalization, physiological training, etc., will be sent to the Repository. The Department of Cardiology, School of Aviation Medicine, will give special cognizance to the tracings taken on the 40th, 45th, 50th, 55th and 60th birthdays and to the records of selectees for flying training. The School will be able to act as a source of reference for individual problem cases. We expect that it will develop data of statistical significance and carry on research with this background material.

Unexplained Syncope

The fourth and concluding problem is that in the Air Force we have a group of flying people, some of whom could be in control of high performance aircraft, who pose a serious problem to us. It involves those who have an episode of syncope for which there is no apparent cause such as hypoglycemia, carotid sinus sensitivity, coughing, posture, salt loss, vasovagal instability, epilepsy or its equivalent, hyperventilation, etc. (Most of these conditions are disqualifying for flying duty in their own right.) In the calendar year 1956, 37 cases of unexplained syncope were handled at Headquarters United States Air Force level. They were suspended from flying duty for obvious reason.

Research in this area is being performed at the School of Aviation Medicine with use of the tilt table and simultaneous recording of the electroencephalogram and electrocardiogram. Preliminary investigation discloses evidence of a central neurocirculatory instability in some of these cases. Research is also being done at the Aero Medical Laboratory where individual tolerance to neurocirculatory stresses are being evaluated by use of the recording electroencephalograph and electrocardiograph under conditions of lowered oxygen tension, "G" forces and artificially induced psychological stress. It is hoped that eventually we will have better parameters to measure such loss of consciousness.

Conclusions

In conclusion, the Air Force has a serious equity in the epidemiologic and prophylactic aspects of both coronary artery disease and rheumatic fever. It has the background material to make longitudinal correlations between electrocardiographic findings and clinical heart disease. The problem of unexplained momentary loss of consciousness in flying personnel presents a challenge with which there can be no equivocation.

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Experimental Studies

The Role of the Endothelium in Acute Pulmonary Edema*

An Electron Microscopic Study

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THE BASIC mechanism of the transudation of liquid into the finest air channels of the lungs in pulmonary edema is still unknown. Many of the contributing factors to such a condition are supposed to produce a hypertension in the capillaries of the lungs. This concept may be one of the reasons for the prevalent opinion that the transudation of liquids into the lungs is due to a permeation of liquid from the capillaries into the air-filled spaces of the alveoli and alveolar ducts.

Having been concerned for a long time with the physiology and pathology of the lungs and with the application of electron microscopy to the solution of these problems, the author has produced pulmonary edema experimentally in the rabbit with the well known method of epinephrine application. The lungs with acute edema have been investigated by means of electron microscopy. The pictures have been compared with corresponding ones of the same tissue of normal animals. A detailed report on these findings will be published in a forthcoming issue (Vol. XVI) of *Experimental Medicine and Surgery*, now in press.

Only one of the main results is shown in the accompanying illustrations. They prove clearly that in acute pulmonary edema produced with the epinephrine method in a normal young rabbit the endothelium of the lung (its ciliated and non-ciliated cells) show an abundant discharge of droplets which are not seen in such excessive amounts in the normal lungs. Apparently, the cells designated previously as specific cells of the lungs do not take part in this process. The secreted droplets separate from the cells, melt together to make bigger ones and are apparently moved ahead by the cilia. Figure 1 shows two cells, a ciliated and a non-ciliated one both in the stage of producing such droplets. Figure 2 shows such bigger droplets already separated from the cells now floating in the smallest air ducts (alveolar ducts) in the lungs, finally interfering with the exchange of air in these ducts. The secreted droplets are precipitated (fixated) and slightly stained by Osmium. They therefore cannot be water but rather a dilute solution of proteins or mucous. For further details readers are referred to the extensive paper to be published.

This presentation proves the remarkable fact that both the ciliated and the unciliated cells of the endothelium in the finest air ducts have a secretory function and that this function present but not very significant in normal animals plays an apparently important role in the production of acute pulmonary edema.

This observation which of course has to be verified by a host of future experiments but seems to lead to a new aspect in our knowledge about

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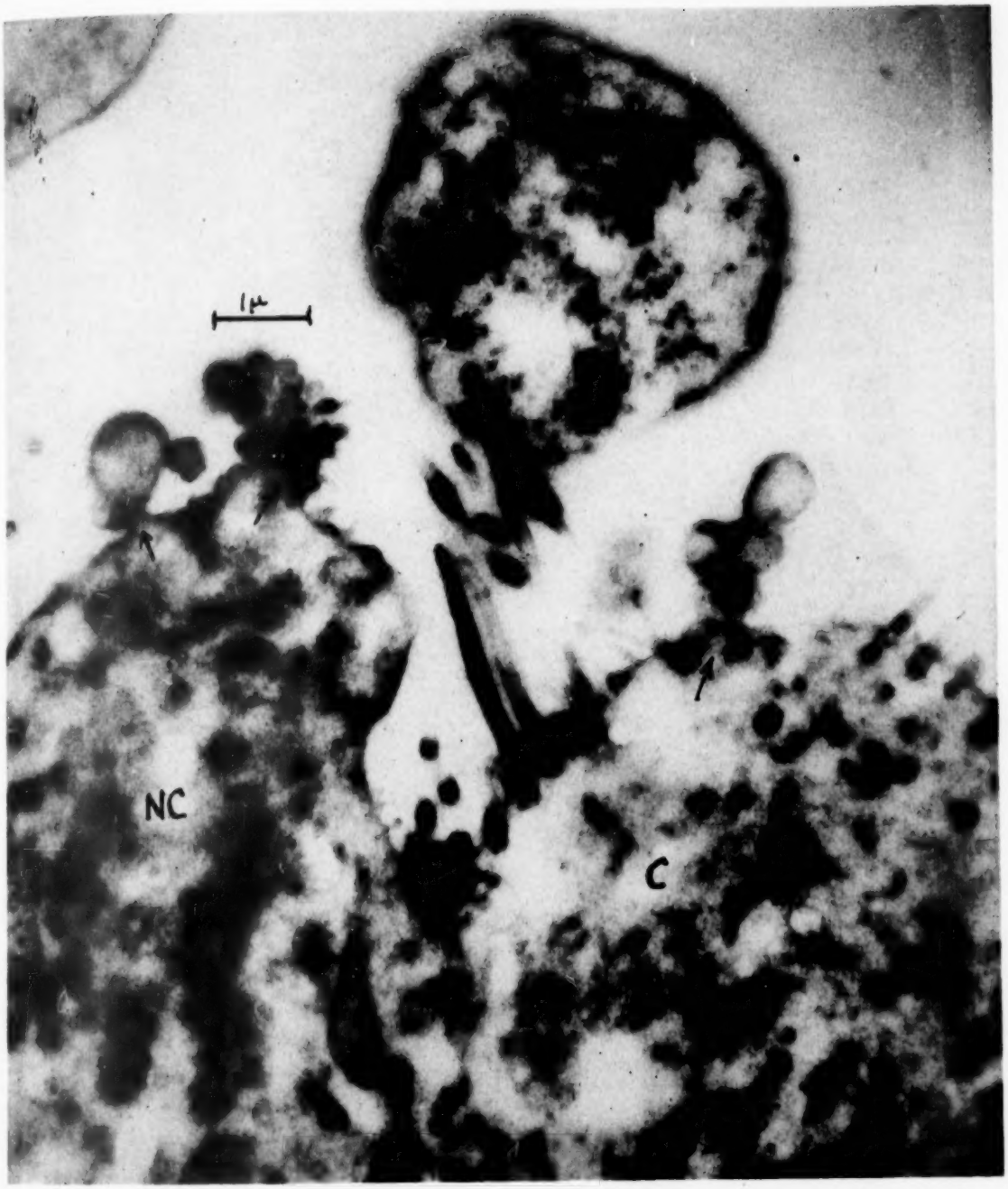

Fig. 1. Lung of a rabbit in acute pulmonary edema. Section from subpleural particle of the lung showing a ciliated (C) and a non-ciliated (NC) cell, both producing small droplets of liquid which as can be seen are still partly connected with the cell (indicated by arrows). The much bigger droplet on top not connected with the cilia is probably not a particle of a cell but rather the result of the fusion of small droplets. Magnification × 15,000.

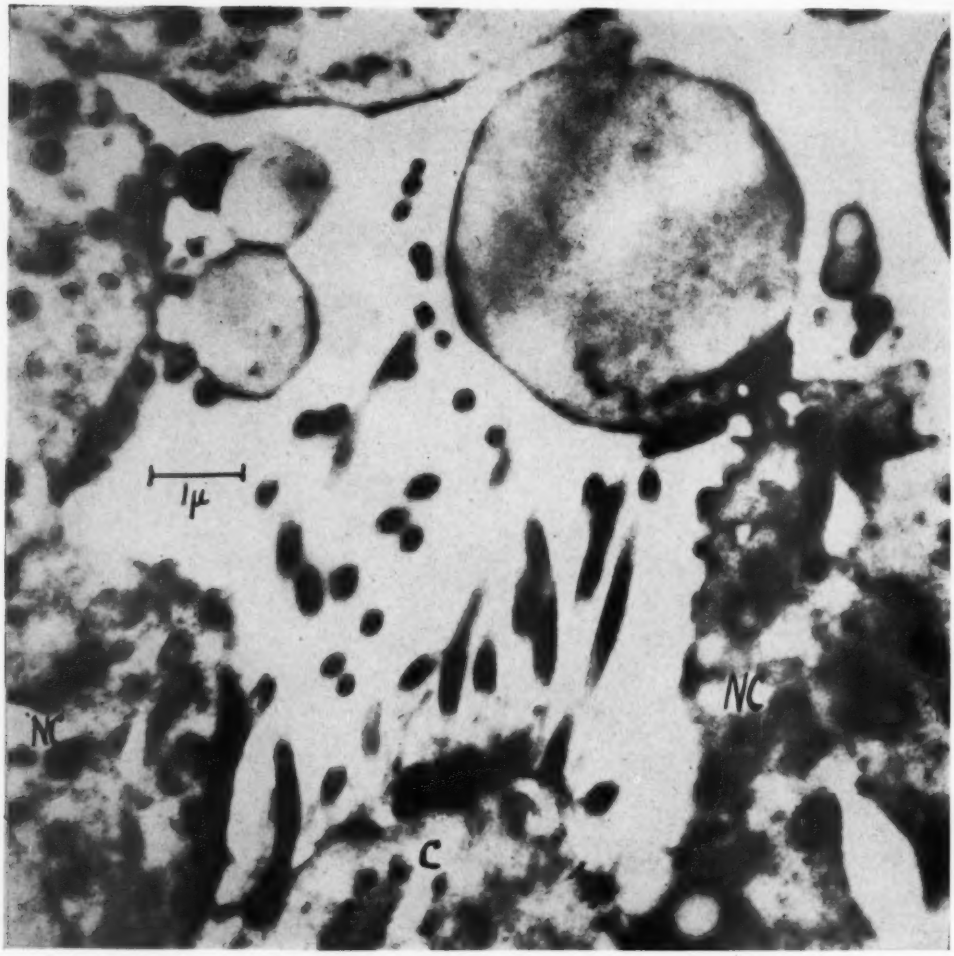

Fig. 2. Section from same particle of the lung as in Figure 1 showing a ciliated cell (C) accosted by two non-ciliated (NC) ones. Bigger and smaller droplets are seen still partly connected with the cells. Magnification × 13,000.

the production of fluid in pulmonary edema may eventually lead to new therapeutic applications.

The changes in the endothelium of the capillaries and the epithelium in the alveoli in pulmonary edema are being reported in the paper in press in *Experimental Medicine and Surgery*.

SUMMARY

An abundant secretion of ciliated and non-ciliated epithelial cells in the smallest air ducts has been demonstrated in the rabbit in experimental acute pulmonary edema. Such secretion is present normally too but in a much lesser degree.

Reports on Therapy

The Role of Ataraxics in Cardiology

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THE ATTENTION of cardiologists in recent years has been focused with increasing clarity on the emotional components of the disorders brought to them for treatment.[1,2] Because of the mental unrest that complicates the clinical picture, it is often difficult for the physician to determine the actual severity of the somatic disease.

Most patients with cardiovascular complaints are fundamentally normal in the psychologic sphere, but, especially in urban localities, live constantly under a degree of tension which may exceed the limits of tolerance in a sudden crisis, as physical disability, grief, loss or some other misfortune. My experience, derived from several years of practice in a large, heavily populated metropolitan area, leads me to estimate that at least 80 per cent of office patients suffer from anxiety severe enough to intensify and prolong their bodily illnesses.

In diagnosis and treatment, therefore, the physician must deal with both the emotional and physical components of the problem simultaneously.[3] Handling of these patients requires *time*,[4] first of all, to probe for the underlying contributing factors as well as the actual physical causes of symptoms; and careful judgment and patience in carrying out treatment. The first principle is to *listen;*[5] the second, to take the positive psychotherapeutic approach: "You can rely on me; I will help you. Very soon you will begin to feel better." The third is not only to attack the somatic disturbance with appropriate therapeutic measures, but also to relieve the emotional tension with a suitable ataractic agent.[6]

Occurrence of side effects from any medication is of great importance to office patients, since they usually undergo treatment while leading active workaday lives, and would be seriously inconvenienced by adverse reactions of any sort.

Meprobamate,* a close relative of mephenesin, which has been used as a general muscle relaxant[7] and to control the milder forms of emotional tension,[8–12] appears to be very suitable for routine use in outpatients.[11] In the molecular structure of the compound, the substitutions in the radical produce more prolonged activity than that obtainable from mephenesin. Furthermore meprobamate is effective by the oral route; mephenesin is not. Meprobamate interrupts abnormal stimuli, chiefly in the internuncial circuits of the subcortical regions, and especially impulses between the cortex and thalamus. The compound has no significant effects on the autonomic nervous system (heart beat, respiration, gastric secretion, and perspiration). Subacute and chronic toxicologic studies and various clinical reports have indicated a very low toxicity (the compound is approximately one-fifth as toxic as most barbiturates).[12]

CLINICAL MATERIAL

Observations were recorded on a series of 41 patients seen over a period of several months in the office or initially in their homes (Table I). Twelve had survived one or more attacks of coronary thrombosis, twelve were suffering from coronary insufficiency; in fourteen labile essential hypertension was the primary diagnosis (eight were women in the menopause and six were extremely obese males); and three showed symptoms of severe cardiac neurosis.

In all cases severe tension and anxiety compli-

* Meprobamate is available as Equanil® from Wyeth Laboratories.

Control of Emotional Complications with Meprobamate in 41 Office Patients

Diagnosis	Number of patients	Meprobamate medication				Additional medication	Remarks
		Initial dosage		Final dosage			
		mg	Schedule	mg	Schedule		
Postcoronary thrombosis (9 males, 3 females, 40 to 52 years old. Initial attacks occurred 2 months to 6 years previously)	12	400	q.i.d. or t.i.d. p.c. (2 months)	200	b.i.d. p.c. (3 months) then p.r.n.	Digitalis, diuretics as required. Nitrites for chest pain, first in 1/3 usual dosage, then discontinued	No barbiturates, reserpine, or antispasmodics. No change in blood pressure or pulse rate, no toxic reactions
Coronary insufficiency (11 males, 1 female, 46 to 58 years old; symptoms 1 1/2 to 3 1/2 years)	12	400	q.i.d. or t.i.d. p.c.	200	b.i.d. p.c. then p.r.n.	Nitrites, first in 1/3 usual dosage, then discontinued	No barbiturates or amphetamines
Labile essential hypertension							
Menopausal syndrome with globus hystericus (42 to 55 years old)	8	400	t.i.d. p.c.	200	t.i.d. p.c. then h.s.	Low sodium or low caloric diet as required. Antihypertensive agents, in reduced dosage, as necessary	Patients with globus hystericus received carbromal, 1 1/2 gr for 2 weeks initially. No other sedatives or hypnotics
Obesity (males, 32 to 50 years)	6			400			
Cardiac neurosis (2 females, 46 and 51 years, 1 male, 40 years)	3	400	q.i.d. or t.i.d. p.c.	200	t.i.d. p.c. then p.r.n.	None	Symptoms subsided on reassurance and control of emotional tension

cated the physical disorder and interfered with satisfactory management of the case. It was clear that response to specific treatment depended to a large extent on alleviation of the associated emotional distress. Rapid control of the psychologic factors in each case was therefore essential.

Medication with meprobamate was begun, in appropriate dosage, usually administered after meals, and was gradually tapered off as the patient became relaxed and responsive to specific measures as indicated. Ataractic treatment was continued for two months to one year; some patients in this series are still receiving the compound in small, widely spaced, doses.

POSTCORONARY THROMBOSIS AND CORONARY INSUFFICIENCY

No medication of any kind, of course, will reverse the damage produced by the coronary episode. The gravity of the situation is intensified by the unavoidable realization by the patient of the seriousness of his problem. He usually becomes "heart conscious" and afraid to resume a normal life. It is essential, therefore, to allay his nervous tension as soon as possible in addition to controlling his physical symptoms (anginal pain and the distress induced by fear are often difficult to differentiate). After an uncomplicated myocardial infarction the patient should not be permitted to become a chronic invalid.[13] It is important to counteract, by erasing the emotional component, the disabling cardiac neurosis that so often follows an acute attack.[14,15]

After discharge from the hospital or release from bedrest at home, meprobamate should be started immediately, in conjunction with the usual specific therapy. The nitrites may temporarily dilate the coronary vessels but do not allay the emotional tension associated with precordial pain. Under properly regulated ataractic medication, the dosage of coronary vasodilators may be radically reduced and in many cases finally eliminated. For instance, 400 mg meprobamate may be taken at appropriate intervals before any situation in which increased tension is anticipated. Thus anginal pain often may be forestalled with no other treatment. One postcoronary patient in this series who often speaks at public gatherings takes 400 mg meprobamate two hours before and 400 mg immedi-

ately prior to the time scheduled for delivery of his speech.

POSTCORONARY THROMBOSIS

CASE 1. A 48-year-old salesman had suffered a coronary occlusion with myocardial infarction eight months previously. Medication had included phenobarbital, reserpine, and antispasmodics, with unfavorable results. He continued to be tense, nervous, apprehensive, and depressed, and was unable to sleep. All his attention was centered on the impairment of his heart and he took no interest in work or diversion. He started on 400 mg meprobamate four times a day; all other medication was stopped. He promptly lost his tenseness and depression, and became more cooperative, slept soundly, was less anxious about his heart, and showed a renewed interest in former activities.

Meprobamate medication was continued for two months at the initial dosage, after which the dose was reduced to 200 mg three times a day with 400 mg at bedtime. This schedule was continued for an additional ten weeks, after which the dose was again reduced to 200 mg twice a day. The patient resumed work on a restricted schedule in a few more weeks, and now takes meprobamate, in doses of 200 mg, only when he is under unusual strain.

CASE 2. A 48-year-old male clothing cutter had been accustomed to take nitroglycerine sublingually for coronary insufficiency throughout a three and one-half year period. He was very nervous and tense under the strain of his job, and complained of frequent precordial pain, palpitation, and insomnia. Meprobamate relaxed his emotional tension, thereby controlling his symptoms and permitting discontinuance of nitroglycerine.

ESSENTIAL HYPERTENSION

It is commonly acknowledged that essential hypertension is a sequel to life stress.[16] Meprobamate is of great value for relief of the anxiety contributing to the mild and moderate cases of labile essential hypertension. The patient usually relates a long history of emotional extremes as irritability, palpitation, headaches, dizziness, and insomnia. His sighing respirations, indicative of hyperventilation, are often noticeable immediately on entrance to the office. Definite symptomatic improvement follows addition of meprobamate to the conventional regimen of antihypertensive medication and appropriate dietary restrictions. When the full calming effect of the compound is achieved there is a commensurate lowering of the blood pressure.

Hypertension is not uncommon in the menopause. The tearful, fatigued, middle-aged woman, with ill-defined fears, illogical worries, vasomotor disturbances, and elevated blood pressure is a frequent visitor to the consulting room of the general practitioner. A functional globus hystericus may be associated.[17] On elimination of emotional tension the clinical picture becomes much different.

CASE 3. A 38-year-old widowed secretary had a history of essential hypertension, with depression, cardiac palpitation, headache, severe insomnia, and occasional globus hystericus since the death of her husband four years previous. She had been under treatment with antihypertensive drugs, barbiturates, and amphetamine for three and one-half years; and when first seen was exceedingly anxious, emotional, and complained of a "lump" in her throat. All barbiturates formerly included in the regimen were eliminated at once. A bedtime dose of Carbrital®, 1 1/2 grains, was instituted for two weeks, to aid in overcoming her resistant insomnia. Meprobamate, 400 mg three times a day, was begun and later reduced to 200 mg at the same intervals. Antihypertensive medication also was reduced. Eventually she was able to do well on no treatment but a bedtime dose of 400 mg meprobamate taken only when she felt particularly tense.

The obese patient with elevated blood pressure is usually seeking an outlet for worry or unhappiness in overeating. Relief of the nervous stress with meprobamate eliminates the abnormal craving for food; hence the patient finds more tolerable the necessary reduction of food intake. In the six obese patients listed (Table I) the blood pressure at start of medication ranged from 178 to 195 systolic, and 85 to 100 diastolic. After brief therapy with meprobamate and regulation of the diet, the pressure levels fell to 140 to 155 systolic, and 80 to 90 diastolic. With complete change in mood under the influence of the ataractic medication, they adjusted easily to the dietary restraints prescribed.

CARDIAC NEUROSIS

CASE 4. A 46-year-old married woman had suffered from nervousness, depression, anxiety, and restlessness for five and one-half months. She could not sleep because of the palpitation, tachycardia, dyspnea, and was obsessed with a fear that her heart would stop beating. After examination, the patient was assured that she had no heart disease, the situation was fully explained to her and she was given 800 mg meprobamate immediately. The compound was continued in doses of 400 mg three times a day, after meals, and at bedtime for a week. The dosage was then reduced to

200 mg three times a day, with 400 mg at bedtime, for four weeks; and finally 200 mg was administered after breakfast and at supper. Her symptoms have completely subsided.

CASE 5. A 40-year-old salesman had been complaining of pain over his heart, lightheadedness, and weakness since the sudden death of his brother-in-law from coronary thrombosis three months previously. The symptoms were not associated with effort, meals, changes in temperature, or excitement; he just had a fear of dying. Findings on physical examination were within normal limits. Meprobamate was administered in doses of 400 mg three times a day for three days, then 200 mg three times a day for six weeks. The patient was reassured that he had no heart abnormalities, and time was taken to explain his "pain." He completely recovered after ten days, but was advised to take meprobamate as required whenever the symptoms recurred.

CASE 6. A 51-year-old married woman, in the menopause, complained of moderately severe "hot flashes" associated with a sensation of "missed beat" in her chest, that had persisted for three and a half months. She was extremely nervous and tense because of the sudden "empty feeling over the chest" whenever the symptom occurred. No organic heart disease could be detected on examination; the diagnosis was of extrasystole on a functional basis. Meprobamate 400 mg four times a day, was continued for ten days. After five days, the extrasystoles disappeared and she felt relaxed. The dose was reduced to 200 mg four times a day, and continued for two months. The patient was soon able to resume her household duties and is no longer "heart conscious."

SIDE EFFECTS

Neither agitation nor depression attended meprobamate medication in this entire series, nor were there any cutaneous or other evidences of sensitivity. A few patients reported yawning and some lassitude in the initial stages, which ceased as treatment progressed. None experienced the somnolence characteristic of conventional sedation with cortical depressants. The soporific effects common to treatment with reserpine and the barbiturates did not develop during use of meprobamate. There was no adverse effect on the blood pressure.

SUMMARY

In at least 80 per cent of the patients seen by the cardiologist, anxiety prolongs and intensifies the physical disorder. The prognosis depends largely on the ability of the physician to control the anxiety factor, as well as the somatic disease. For ambulatory patients, meprobamate is believed the most suitable of the ataractic agents for this purpose.

A series of 41 adult patients who had survived one or more episodes of coronary thrombosis, or were suffering from coronary insufficiency, labile essential hypertension, or cardiac neurosis, received meprobamate in initial doses usually of 400 mg, three or four times a day, in conjunction with the appropriate specific therapy. On control of the acute symptoms dosage was halved, and administered at longer intervals. Medication was continued from two months to one year. On control of the emotional complications, treatment in every case was less intensive and prolonged than ordinarily would have been expected. The postcoronary and hypertensive patients were less apprehensive and excitable, and convalescence was more rapid.

Drowsiness in the first few days of medication occurred in a few but subsided with no reduction in dosage. Meprobamate is essentially nontoxic and therefore well suited for prolonged treatment in chronic disorders with emotional complications.

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Use of Dioctyl Sodium Sulfosuccinate in Cardiovascular Disease*

Correction of Bowel Function

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THE SPECIALIST in cardiovascular disease cannot divorce himself from the problems of bowel function even though he is not primarily concerned with the subject of gastroenterology. In addition to the inordinate interest in bowel function displayed by most patients, there are important and serious problems of bowel management which arise in the bedfast cardiac patient.

A number of factors increase the tendency to constipation and even obstipation in such patients. For instance, patients with acute myocardial infarction or acute pulmonary edema are usually given morphine which exerts a depressing effect on the gastrointestinal tract. In decompensation, the anoxic edematous bowel wall is functionally sluggish and shares to some extent in the pattern of right heart failure. The very action of putting a patient to bed invites constipation through loss of muscular tone in the abdominal wall. The use of dehydrating agents invites constipation in chronic passive congestion because of their lack of selective action. Furthermore, cardiac patients tend to be in the middle and older age group where constipation is quite commonly an increasing problem. It must also be noted that psychosomatic aspects are involved. Fear and apprehension in the patient faced with the reality of a serious heart attack may cause a spastic condition.

Most cardiac patients, therefore, have a pronounced tendency toward constipation and it is in these very patients that the condition may be extremely dangerous in inviting complications and aggravation of their pathology.

Where pulmonary embolism or pulmonary infarction exists, or where a thrombus may be present in a heart chamber or in the veins of the legs or pelvic area, straining at the stool as a result of constipation or impaction may be dangerous. As Marple and Wright[1] have pointed out, straining changes intrathoracic pressures and a potentially dangerous "sucking" action on thrombi may result. This may lead to catastrophe in the patient who has had one embolic accident and by straining may develop a second embolic accident which is often massive or lethal. Furthermore, as Friedberg[2] has noted, straining at stool may also frequently result in the development of initial pulmonary embolization.

Following acute myocardial infarction a temporary period of constipation is in some ways desirable. Friedberg[3] has emphasized the undesirability of disturbing the patient or of encouraging a bowel movement for the first three days following a severe cardiac "attack." Spontaneous bowel evacuation does not usually occur during this period because of low food intake and because of the administration of opiates.

The initial bowel movement following acute myocardial infarction, however, is a source of fear and apprehension both to the patient and his physician. Usually four or five days have elapsed without bowel movement. The subsequent ordeal of straining on the bedpan invites rupture of the ventricle or of "firing off" an embolus from the mural thrombus at the site of the transmural infarction. Patients have died on the bedpan; patients have had emboli on

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the bedpan; patients have had ventricular rupture on the bedpan; and patients have gone into cardiogenic shock on the bedpan. Nevertheless, many patients are simply too ill to be permitted bathroom privileges or even to be lifted to a bedside commode.

All of the considerations outlined above explain the interest of the cardiologist in reducing the effort, stress and strain of fecal elimination in cardiac patients. Certainly, the development of constipation and the manual relief of impaction, as recommended by Friedberg,[3] should be avoided if possible. Not only do abdominal distress and distention place an added burden upon the heart but it is well known that distention of the rectum exerts a strong cardiorespiratory stimulant action which is exceedingly undesirable in the patient whose heart is in jeopardy.

Obviously, an agent which could be started promptly after a cardiac attack and which would ultimately result in a soft initial stool but which would be free of irritant laxative action would be most desirable. A satisfactory regiment of treatment which would result in easy passage of a soft stool without strain would be a boon both to the patient and to the cardiologist.

The recent introduction of dioctyl sodium sulfosuccinate* has changed many of the older concepts in the treatment of constipation. The therapeutic value of this drug has been reported in constipation in various types of patients. Cass and Frederik[4] and Spiesman and Malow[5] reported its effects in chronic atonic and in spastic constipation. Phelps[6] studied its effectiveness in mental patients. Harris[7] and Wilson and Dickinson[8] investigated its use in elderly or immobilized patients. Turell[9] found it to be useful after anorectal surgery. Middleton[10] was impressed with its effectiveness in postpartum patients.

The action of dioctyl sodium sulfosuccinate is based upon a purely physical phenomenon which results in a reduction of interfacial tension between the immiscible phases of the heterogeneous fecal material. A soft, homogeneous fecal mass results and easy passage of the softened stool occurs. Unlike ordinary laxative agents, dioctyl sodium sulfosuccinate does not cause bowel movement nor does it affect, in any way, the normal water balance of the body.

The bowel properties of this new fecal softener appear to meet the requirements of the ideal agent for use in cardiac patients. Lack of laxative action and maintenance of a soft fecal mass during the period of required bowel inactivity are important considerations. Elimination of the tendency to impaction and the dangers of straining at the stool could be life-saving. Absence of interference with body water balance is a highly desirable property.

Material and Methods

We have used dioctyl sodium sulfosuccinate in four groups of patients. The first group consisted of 50 patients with classic acute transmural myocardial infarction occurring as a result of coronary arteriosclerosis with occlusion.

The second group consisted of 20 patients in whom pulmonary emboli had resulted in pulmonary infarction. A mural thrombus in the heart or thrombosis in the veins of the legs or pelvis was doubtless the original seat of embolization.

The third group of 18 patients required bedrest because of severe cardiac decompensation. These patients were already constipated because of an edematous, sluggish gastrointestinal tract. Some of these patients exhibited the paradox of localized tissue edema in some regions and tissue dehydration in other areas. In some cases mercurial diuretics had apparently reduced the water content of the intestinal fluids.

The fourth group consisted of 15 cardiac patients of various types and descriptions who were bedfast and in whom maintenance of normal bowel function seemed desirable to avoid exacerbation of the existing cardiac condition.

In all of the patients described above we administered one doxinate 240 mg capsule once daily. This therapy was begun routinely beginning on the first day of hospitalization. It was continued throughout the hospital stay. In previous preliminary tests, lower dosages had proved to be much less efficacious than those described in this report.

* Dioctyl sodium sulfosuccinate used in this study is marketed as Doxinate® 240 mg by Lloyd Brothers, Inc., Cincinnati, Ohio in the form of soft gelatin capsules.

Results

Results in all four types of patients were uniformly excellent. Objective measures for an evaluation of this type are not available and it is necessary, therefore, that our opinion be based upon a comparison with past experience. Nevertheless, it was observed that milk of magnesia with mineral oil as a laxative was rarely ordered for these patients and that saline enemas were seldom necessary. These observations are in contrast to previous experience where both forms of treatment were commonly required.

In our evaluation, patients often spontaneously expressed complete satisfaction with their bowel function and unsolicited comments on the ease and smoothness of fecal elimination were of frequent occurrence although these patients did not know that any preventive therapeutic regimen had been undertaken. Comments of one patient, a general practitioner, who had seen death from vigorous enemas or relief of fecal impaction in patients after myocardial infarction, were especially noteworthy in this respect.

The average duration of hospitalization of the patients in our group after acute transmural myocardial infarction was from 21 to 35 days depending on the severity of the case. In these 50 cases we have observed no single instance of impaction during the three to four-month period of our study.

In a general way, all patients included in our study received beneficial effects from the use of dioctyl sodium sulfosuccinate. Straining on the bedpan was greatly reduced. No toxicity was noted at any time. No allergic reactions were seen. In a few cases where broad-spectrum antibiotics were also used, the consistency of the soft stool was not altered even though such agents commonly cause a loose, watery evacuation.

In the patients treated with dioctyl sodium sulfosuccinate very few reported or were observed to have any marked difficulty with bowel function. The need for enemas and traditional laxative measures was practically eliminated. The consistency of the stool was uniformly soft and evacuation was greatly eased. Patient cooperation was excellent. In patients with acute myocardial infarction no effect on the desirable delay in the initial movement was seen.

We also have used dioctyl sodium sulfosuccinate in a very limited way in patients following cerebrovascular accident since many of the same considerations apply in these patients. At this time our study is not sufficiently broad to permit conclusions to be reached but further studies in patients of this type are indicated.

Case Histories

Among the many interesting cases in our study we describe briefly three rather typical ones.

Case 1. The patient, a physician, suffered considerable anxiety concerning hospitalization for myocardial infarction because of a pre-existing difficult bowel problem. It was his intention to follow his own regimen of bathroom privileges, bedside commode and use of laxation. Through the influence of his two sons, who were physicians, he was admitted to the hospital and immediately put on doxinate 240 mg, one capsule daily. At no time during his 28-day stay at the hospital was he troubled with bowel function and he was high in his praise of the favorable effect of this agent and of the satisfaction he received upon the correction of his bowel problem. He has continued satisfactorily on 120 mg of doxinate since discharge from the hospital.

Case 2. A critically ill patient who had had two major myocardial infarctions and one minor infarction was admitted to the hospital with acute myocardial infarction accompanied by excruciating pain. The patient promptly went into congestive heart failure followed by paroxysmal atrial fibrillation and later by a small pulmonary infarction. The patient had experienced repeated episodes of constipation at each previous hospitalization. In this case the use of doxinate 240 mg once daily eliminated any need for enemas or laxatives during the period of hospitalization although at times the patient was critically and seriously ill.

Case 3. The patient had a combined anterior and posterior myocardial infarction. He rebelled strongly at hospitalization and bedrest. Because of his fear of constipation and impaction he got up and walked to the toilet on several occasions without approval. When the doxinate 240 mg regimen was instituted, bowel movement occurred with ease and regularity and eliminated the patient's anxiety complex. At the end of his visit he expressed great satisfaction with the result of treatment. He has continued on this medication since his discharge and a recent office re-evaluation elicited no bowel difficulty.

Discussion

We have pointed out that constipation is an important consideration to the cardiologist. It is of sufficient importance so that most reference works include sections on the treatment

of constipation in cardiac patients. For example, Hellerstein[11] has outlined one of the commonly accepted methods of bowel care. Following acute myocardial infarction he recommends low dietary intake for several days, adequate fluids and subsequent mild laxation. If bowel movement does not occur by the third or fourth day a glycerine suppository or glycerine enemas are advised.

Our previous technic in handling the problem of bowel function was to administer a mixture containing mineral oil and milk of magnesia on the third day. In the absence of bowel movement on the fourth or fifth day a saline enema was given. Subsequently, mineral oil and milk of magnesia were given orally and enemas were used as necessary. In our experience the use of dioctyl sodium sulfosuccinate practically replaces our previous method of handling this problem. It is more effective and its use offers important advantages both to the patient and to the cardiologist. It is our considered opinion that the relief from straining at the stool is, in many instances, life-saving.

Tangible benefits from this new method of treatment are present for both the cardiologist and the patient. The cardiologist is primarily concerned with cardiac function and low morbidity and it is not an inconsiderable advantage to avoid time-consuming and perhaps inconsequential discussions of difficulty in bowel function. Furthermore, it is worthwhile to eliminate the anxiety which must be present when severe constipation is a potential danger.

Since surface tension changes in the lumen of the intestine occur with the administration of dioctyl sodium sulfosuccinate it is conceivable that the absorption of other medicaments might be altered. This is an important point since the oral administration of anticoagulants such as dicumerol has become accepted therapy following acute myocardial infarction. Our observations indicate that our usual dosage schedule for dicumerol was not affected and that it was equally effective when given in combination with doxinate.

Summary

We have studied the application of fecal softening (doxinate) as a means of avoiding some of the dangers which accompany the appearance of constipation in cardiac patients. Our observations were made in 103 patients with classic acute transmural myocardial infarction due to coronary occlusion, pulmonary emboli resulting in pulmonary infarction, cardiac decompensation and other cardiovascular conditions resulting in hospitalization.

Results were excellent in all cases and the avoidance of impaction and straining on defecation not only helps the cardiologist treating the patient, but may actually save the life of the patient.

Our regimen of treatment consists in the administration of one doxinate 240 mg capsule daily throughout the period of hospital stay for all patients. In our practice this procedure has been so effective and patient satisfaction has been so great that it has almost entirely replaced the use of laxatives and enemas. In our experience no evidence of undesirable effects or toxicity were noted.

In the handling of bowel problems in cardiac patients, the properties of dioctyl sodium sulfosuccinate closely approach those required of an ideal agent.

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Case Report

Congenital Ventriculo-Atrial Communication with Anomalous Tricuspid Valve*

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Houston, Texas

Left to right intracardiac vascular shunts are most commonly associated with defects of the interventricular or interatrial septa. Less frequently left to right shunts may result from defective embryologic development of the endocardial atrio-ventricular cushions and complicated defects such as atrio-ventriculare commune may result. Such lesions produce shunts between the atria or between the ventricles or both. Rarely a defect occurs between the left ventricle and the right atrium, involving the membranous portion of the ventricular septum and often the tricuspid valve, with production of a left to right ventriculo-atrial shunt. Recently we have studied a patient with ventriculo-atrial shunt and an unusual anomaly of the tricuspid valve which may not have been previously described. The clinical and physiologic findings relative to this patient, together with pertinent observations on similar cases, constitute the basis of this report.

Case History

B. M., a 31-year-old white female was admitted to Jefferson Davis Hospital April 15, 1956. She was known to have a cardiac abnormality since age four years. There was no history of childhood cyanosis, squatting, or retardation of development, although a decreased exercise tolerance through childhood and adulthood had been present. During her second decade the patient had noted at times a discomfort over the left chest and occasional palpitation but was able to carry on the duties of a department store clerk without difficulty. Later she performed routine household work with only a gradual increase in the incidence of palpitation. During the years 1948 through 1951 she had four pregnancies, carrying two to term with only moderate dyspnea. There were two spontaneous abortions. In 1955 a fifth pregnancy was terminated elsewhere by therapeutic abortion followed by tubal ligation because of greatly increased symptoms. Over the past two years the patient had noted a greatly decreased exercise tolerance with severe dyspnea and palpitation on exertion. In December 1955 she was hospitalized elsewhere and treated with oxygen and quinidine following an episode characterized by severe "fluttering" of her heart associated with sweating and weakness. Following this episode, she was referred to Jefferson Davis Hospital for further study and treatment.

Clinical Findings: On examination the blood pressure was 132/74 mm Hg. The pulse was irregular, rate 104. There was cardiac enlargement with the left border of dullness in the mid-axillary line and the right border 2 cm to the right of the sternum. The point of maximum impulse was diffuse, in the left anterior axillary line, fifth intercostal space. A systolic thrill was palpable over the precordium and of greatest intensity to the left of the sternum in the fourth intercostal space. The aortic second sound was slightly louder than the pulmonic second sound, and both were somewhat accentuated. A loud harsh systolic murmur was heard over the precordium with maximum intensity to the left of the sternum in the fourth intercostal space. All peripheral pulses were normal.

Laboratory studies were normal except for a mild anemia. Roentgenograms of the chest (Fig. 1) showed cardiac enlargement, prominence of the pulmonary arterial segment, enlargement of the pulmonary arterial branches, and hypoplasia of the aorta. At fluoroscopy the pulmonary vascular shadows, the pulmonary

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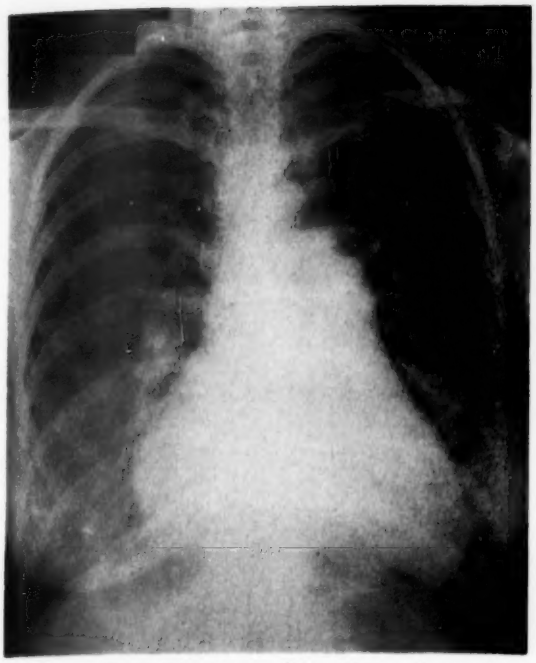

Fig. 1. Roentgenogram of the chest. See text.

arteries, and the undivided portion of the pulmonary artery were more prominent than usual. A definite "hilar dance" was noted. There was right atrial and right ventricular enlargement with a suggestion of left atrial enlargement on barium swallow. The electrocardiogram (Fig. 2) revealed sinus rhythm, complete

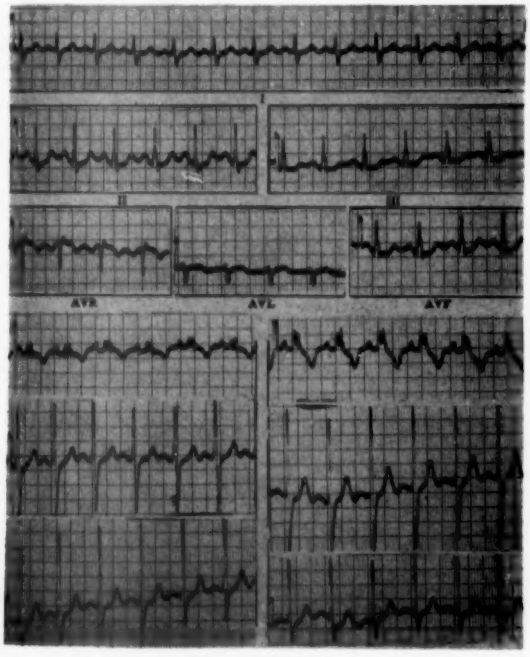

Fig. 2. Electrocardiogram. See text.

right bundle branch block, and tall P waves suggestive of atrial enlargement.

Catheterization Findings: Cardiac catheterization was initially attempted through a left arm vein. On reaching the mid-chest the catheter descended on the left side of the mediastinum to the level of the pulmonary artery. It could not be advanced further, and efforts to do so resulted in the precipitation of multifocal premature beats. These observations suggested a persistent left superior cava emptying into the coronary sinus. Catheterization was then carried out through a right arm vein with the findings noted in Table I. There was a low pulse pressure in the pulmonary artery with a slightly elevated mean pressure. A left to right shunt at the level of the atrium was demonstrated by an increase in oxygen content of the atrial blood as compared with caval blood. The calculated pulmonary blood flow was 1.9 times the systemic flow. No right to left shunt was demonstrated at rest or during exercise. The right atrial pressure tracing was characterized by the presence of a large "c" wave, associated with a fluid venous oscillatory sine wave having a period of about 0.14 sec. Reconstruction of such a sine wave placed in proper phase relation with the recorded atrial pressure pulse, and algebraic summation of the two curves yielded a pressure curve of normal amplitude and configuration for the atrium.

The preoperative diagnosis was interatrial septal defect and persistent left superior vena cava emptying into the coronary sinus.

Operative Findings and Results: Operation was performed on April 20, 1956 under general anesthesia and hypothermia. Body temperature was reduced to 32° F in a cold tub and a bilateral anterior fourth intercostal space incision was made transecting the sternum transversely. The right auricle was distended with oxygenated blood and a palpable thrill was present in the atrium. With a purse string suture above the right auricular appendage digital exploration of the right atrium was carried out. The thrill was originating in the atrium medially near the root of the aorta at the annulus of the tricuspid valve. A septal defect measuring approximately 1.5 cm in diameter was present and the thrill could be eliminated by plugging the defect with the exploring index finger. Because of this, the defect was exposed by a wide right atriotomy incision rather than through the right ventricle. Occluding tapes placed around the superior and inferior vena cavae were drawn tight and as the heart emptied itself of blood, an atraumatic clamp was placed across the base of the aorta and pulmonary artery. The atriotomy incision was made and the septal defect was exposed. The defect was located in the membranous portion of the ventricular septum above the septal leaflet of the tricuspid valve. During ventricular systole, a jet of oxygenated blood spurted from the opening. The defect was closed with three figure of eight silk sutures and the atriotomy was closed after the heart had been flooded with saline to eliminate air bubbles. The period

TABLE I
Results of Cardiac Catheterization

Location	Pressure, mm Hg		O_2 content	O_2 capacity (volume %)	O_2 saturation (%)	Hematocrit
	Systolic/diastolic	Mean				
Right pulmonary artery	26/19	24	13.3	—	—	40.0
Main pulmonary artery	24/17	21	13.2	—	—	39.7
Right ventricle	/1	—	13.7	—	—	39.4
Right atrium	—	0	13.0	—	—	38.5
Superior vena cava	—	—	10.4	—	—	39.6
Inferior vena cava	—	—	10.1	—	—	38.9
Left brachial artery (rest)	128/87	103	15.2	16.2	96	—
Left brachial artery (exercise)	—	—	14.8	16.1	94	—

of circulatory interruption was seven minutes and when the caval flow was restored, cardiac action resumed in a satisfactory fashion. About five minutes later, ventricular tachycardia and ventricular fibrillation suddenly appeared. In spite of all attempts to defibrillate the ventricles using electric shock, procaine amide, and adrenalin, cardiac resuscitation was not possible.

Postmortem Findings: Autopsy was performed one hour after death occurred. The heart weighed 570 g with enlargement of the right atrium and ventricle, the latter averaging 0.7 cm in thickness. There was moderate hypertrophy of the left ventricle which was up to 1.7 cm in thickness. A 0.3- by 4-cm muscular band extended laterally across the right atrium. A 1.2-cm defect just below the annulus fibrosis communicated with the left ventricle at a level just below the right coronary cusp of the aortic valve through the membranous portion of the interventricular septum (Fig. 3). The edges of the defect in the medial leaflet of the tricuspid valve were fused about the orifice of the interventricular septal defect (Fig. 4). There was a 3.5-cm deep saccular outpouching of the medial tricuspid leaflet projecting into the right ventricular outflow tract (Fig. 5). The tricuspid valve measured 15.2 cm in circumference. A minute guarded patent foramen ovale was present. The coronary sinus was dilated and a persistent left superior vena cava emptied into it on the posterior surface of the left atrium. There were three orifices to the right coronary artery but the arterial distribution was normal. The remaining valves were normal as was the origin of the great vessels.

Discussion

The septal defect described here presumably represents an instance of failure of proper development and fusion of the endocardial cushions. McCullough and Wilbur[1] have described a case in which a channel existed between the atrium and the left ventricle at the level of origin of the tricuspid valve after traversing the septum through structures normally formed by the ventral endocardial cushion. Various forms of left ventricular-right atrial communications have been described.[2,3] These may take the form of a defect in the membranous portion of the interventricular septum continuous with a defect in the floor of the right atrium without involving the tricuspid valve, or may be associated with defects in the medial leaflet of the tricuspid valve. If the tricuspid defect is that of a double orifice, the edges of the anoma-

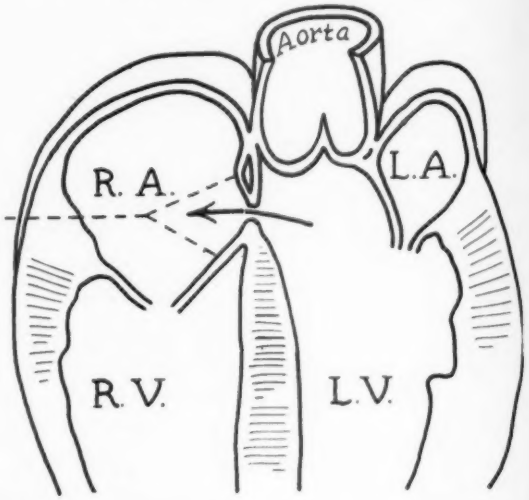

Fig. 3. Drawing of heart in sagittal plane showing the anatomic location of the membranous septal defect producing left ventricular to right atrial intracardiac shunt (arrow). Broken lines show the position of the medial cusp of the tricuspid valve.

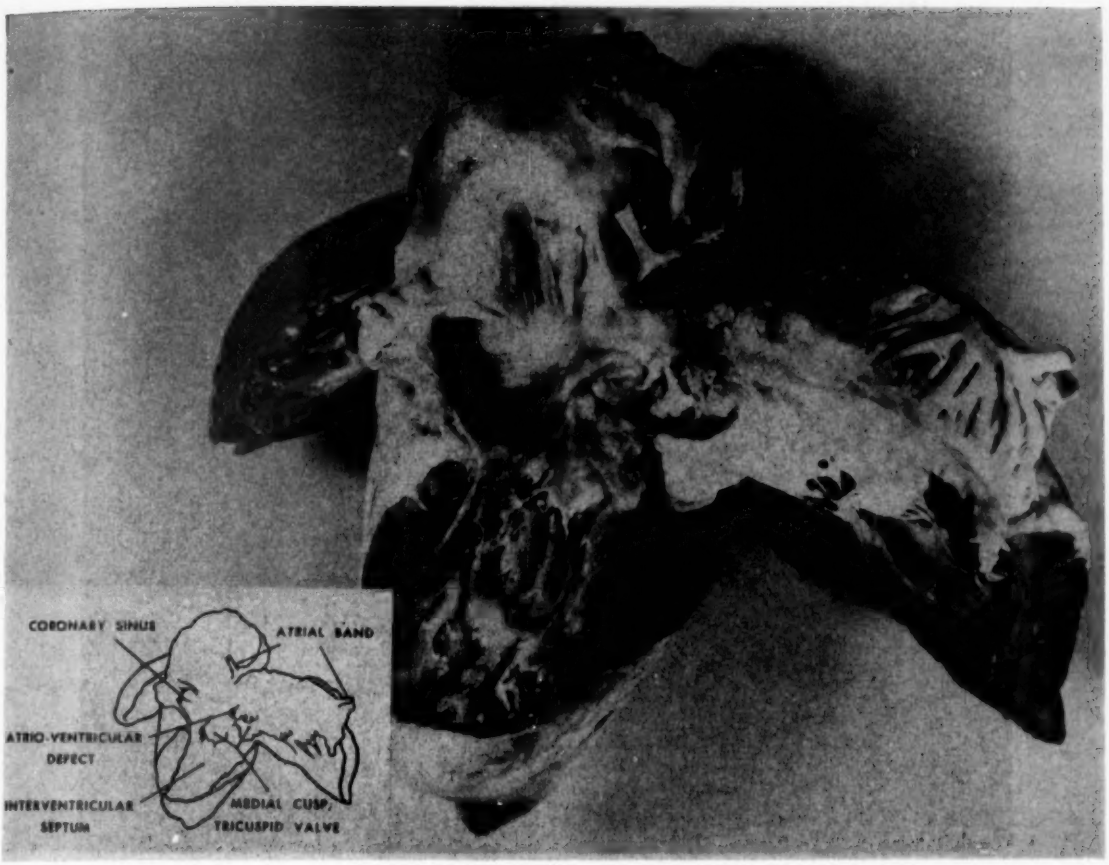

Fig. 4. Photograph of specimen exposing right atrial and right ventricular chambers. The atrio-ventricular defect is demonstrated at the attachment of the medial cusp of the tricuspid valve, with the saccular aneurysm of the valve leaflet extending inferiorly into the right ventricular outflow tract.

lous orifice may be fused to the edges of the septal defect resulting only in a left ventricular-right atrial shunt. However, if the edges are not fused, there results an interventricular shunt with regurgitation through the tricuspid leaflet defect into the right atrium. An additional type of defect is reported by Hemsath, Greenberg, and Shain[4] in which a double defect of the interventricular septum was associated with shortening of the medial cusp of the tricuspid valve resulting in left ventricular-right atrial shunt similar to that reported by Gutzeit.[5] Recently, Stahlman and others[6] have reported two cases of a similar nature with cardiac catheterization, operative, and postmortem findings. In both cases the physical findings revealed cardiac enlargement with a coarse systolic thrill over the left precordium and a loud, harsh systolic murmur along the left sternal border, loudest in one case in the second interspace and in the other in the fourth and fifth, similar to our case. Electrocardiograms revealed incomplete right bundle branch block and right ventricular hypertrophy, respectively, while roentgen examinations showed enlargement of the right ventricle, prominence of the pulmonary artery, and increased pulmonary vascularity in both cases. There was a hypoplastic aortic knob in one case and marked right atrial enlargement in the other. Cardiac catheterization data in these cases revealed pulmonary hypertension, left to right shunt at the level of the right atrium, and in one case a right atrial pressure curve with a prominent "c" wave, interpreted as indicating functional tricuspid insufficiency. The preoperative diagnosis in these cases, as in our case, was interatrial septal defect.

There are several diagnostic possibilities when

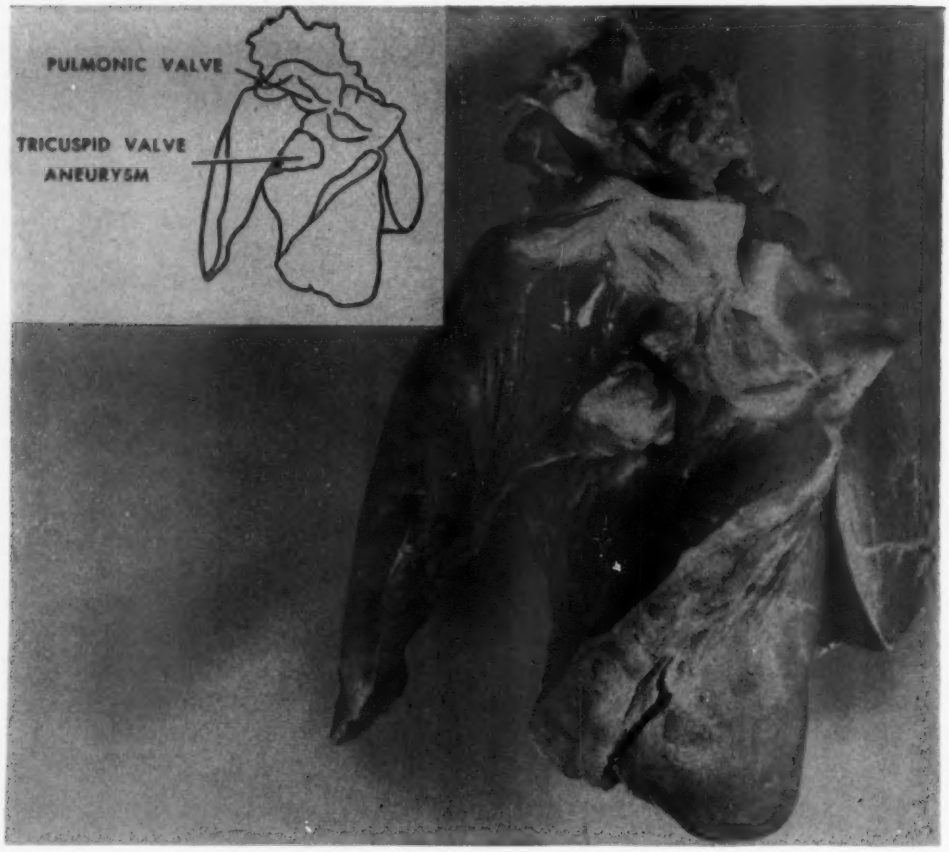

Fig. 5. Photograph of specimen showing the right ventricular outflow tract and the saccular tricuspid valve aneurysm bulging into the ventricular cavity just below the pulmonic valve.

arterialization of right atrial blood is found during cardiac catheterization. However, with the clinical findings present in this case, the chief differential diagnosis included interatrial septal defect, interventricular septal defect with tricuspid insufficiency, and left ventricular-right atrial defect with or without tricuspid valve involvement. In this case, as in those of Stahlman and Perry, a loud harsh systolic murmur was present along the left sternal border maximal in the fourth intercostal space, and accompanied by a systolic thrill. The location of the murmur was somewhat lower over the precordium than is usually found in uncomplicated interatrial defect, and this, together with its loud intensity, might have been a clue to the diagnosis. There was little in the roentgenographic examination or electrocardiogram to differentiate this lesion from that of interatrial defect. The finding of a prominent "c" wave in the right atrial pressure tracing might have been helpful in diagnosis. This alteration in the atrial pressure pulse wave is not characteristic of uncomplicated interatrial defect in our experience. On the other hand, analysis of our tracing yielded no evidence to support the diagnosis of tricuspid insufficiency or other functional abnormality, and sinus tachycardia alone may have given rise to the observed distortion of the curve. Demonstration at operation of a systolic jet of oxygenated blood into the right atrial chamber, associated with a defect in the region of the annulus of the tricuspid valve, revealed the correct diagnosis. Although operation was unsuccessful in this and previously reported cases, recent improvements in open cardiac surgery utilizing extra-corporeal circulation and cardiopulmonary by-pass indicate that such lesions are readily correctible.[7]

So far as we are aware, the findings of a large

saccular aneurysm of the medial tricuspid leaflet in association with this defect has not been previously reported. The possible hemodynamic effects of this bulging sac in the right ventricle cannot be defined in this case. However, it is notable that no significant differential in systolic pressure was found in the right ventricle between tricuspid region and outflow tract at the time of catheterization.

Summary

A case of left ventricular-right atrial communication associated with a saccular aneurysm of the septal leaflet of the tricuspid valve is presented, with inclusion of cardiac catheterization, operative, and postmortem findings. The anatomic defect involved a communication between right atrium and left ventricle at a level just below the right coronary cusp of the aortic valve through the membranous portion of the interventricular septum. Perhaps the most unusual feature of the anomaly was the presence of the deep saccular aneurysm of the septal leaflet of the tricuspid valve at the site of the defect, projecting upward into the outflow tract of the right ventricle.

The preoperative differentiation of this lesion from interatrial septal defect is difficult and the individual differences observed in this case are not specific. However, the combined findings of a loud harsh systolic murmur to the left of the sternum maximal over the lower precordium, and a prominent "c" wave in the atrial pulse pressure tracing are suggestive of a ventriculo-atrial type communication when a left to right shunt exists at the atrial level. The operative demonstration of a systolic jet of oxygenated blood from a defect in the right atrial wall in the region of the tricuspid annulus is presumptive evidence of such a communication. Since the lesion has proved to be surgically correctible, the importance of its recognition is stressed.

Acknowledgment

The authors are indebted to Dr. Joyce Davis of the Department of Pathology, Jefferson Davis Hospital, for the anatomic description.

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Diagnostic Shelf

Pericardial Metastases: Paradoxical Pulse

THE PATIENT,* a 58-year-old negro male steel worker, was admitted to the hospital complaining of epigastric pain of seven months' duration. At first, this was relieved by food, then pain became continuous. The patient lost about 50 pounds in this period. He had been in good health until the onset of pain seven months prior to examination.

The liver was severely enlarged (four fingers below the costal arch) and tender. There was marked resistance and tenderness at the epigastrium. The spleen was barely palpable. There was a positive hepato-jugular reflux.

In the following days, the orthopnea increased, tachycardia was noted (90–120), and the blood pressure was 90/50–120/90.

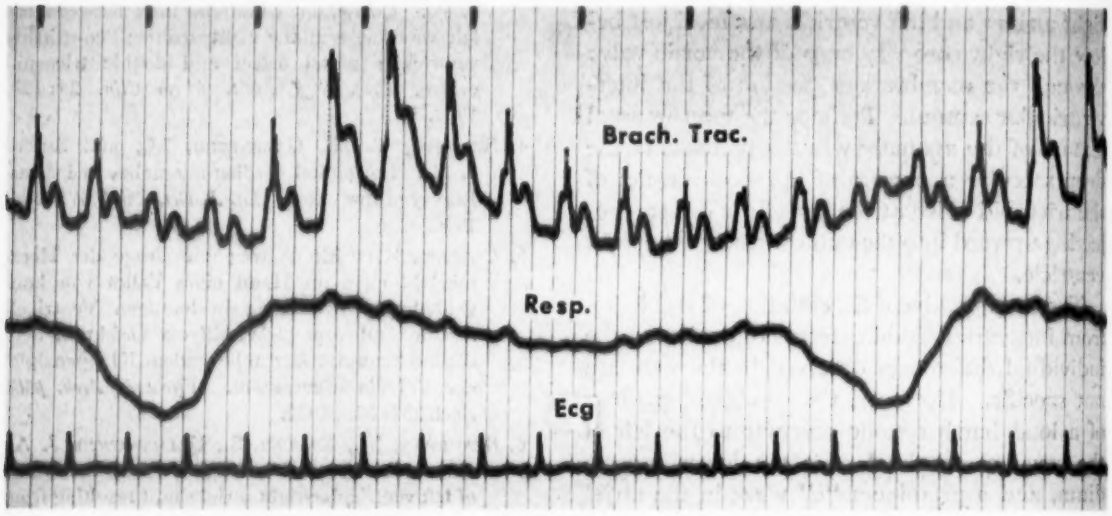

Fig. 1. The brachial pulse tracing shows a paradoxical pulse. The largest pulse waves are seen after expiration. They become smaller during inspiration.

PHYSICAL FINDINGS

Physical examination revealed an emaciated orthopneic man. The pulse was 120, regular, and showed extremely marked respiratory variations. The jugular veins were distended and actively pulsating. There were crepitant rales at both lung bases. Cardiac dullness was greatly enlarged to both sides and shifted with gravity following change in body position. The heart sounds were distant and there were no murmurs.

* Private patient of Dr. A. Bernstein at Mount Sinai Hospital, Chicago, Illinois.

LABORATORY FINDINGS

The laboratory data were as follows:

Stools: Presence of occult blood.

Electrocardiogram: Sinus tachycardia. Slight upward displacement of S-T in the limb leads. Low T waves in all chest leads.

X-ray: Massive globular enlargement of the cardiac shadow. Increase of hilar and vascular markings. Blunting of left costophrenic angle by effusion.

Serum amylase = 44 units. *Urine amylase* = 160.

Left pleural effusion: 1,800 cc of dark red fluid.

Specific gravity 1,012. Malignant cells identified.

Pericardial effusion: 15 cc of dark red fluid. Malignant cells identified. (Subsequent taps removed from 500 to 600 cc.)

CLINICAL DIAGNOSIS

Malignant abdominal tumor, probably pancreatic, with hepatic, pleural, and pericardial metastases.

A brachial pulse tracing was recorded 24 hours after pericardial paracentesis. It revealed a *typical paradoxical pulse* with greatest height of the pulsations *after* the end of expiration (Fig. 1). This led to diagnosis of *pleuropericardial adhesions*. Therefore, the complete clinical diagnosis included pleuritis, pericarditis, and mediastinitis with adhesions.

POSTMORTEM FINDINGS

Autopsy revealed the following:

(1) Carcinoma of tail of pancreas with hepatic metastases. In addition to the nodules, the liver was severely congested.

(2) Mediastinal metastases with enlarged lymph nodes compressing the branches of the pulmonary artery and several of the venous collectors. Diffuse pleuropericardial adhesions.

(3) Hemorrhagic effusions in both pleural cavities and in the pericardial sac.

(4) Metastases in the walls of the right atrium and ventricle.

DISCUSSION

The diagnosis of this case was evident in regard to the primary cause (abdominal malignancy) and to the possible sequelae (hepatic and mediastinal metastases). The existence of neoplastic pleurisy and pericarditis was confirmed by repeated paracenteses.

The typical paradoxical pulse (*Kussmaul's pulse*) led to the suspicion that there might be adhesions between the pericardial sac and the surrounding structures. The brachial artery tracing confirmed that the pulse was typically large *after* expiration and small in all other phases. Autopsy confirmed the existence of external adhesions (accretio cordis) without internal adhesions. It is likely that the paradoxical pulse was enhanced by the solid structure of the mediastinum and by the existence of abundant fluid within the pericardial sac. The latter transmitted more thoroughly any external traction to the heart.

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Symposium on Rheumatic Fever . . . Acute Nonspecific Pericarditis . . . Idiopathic Myocardial Hypertrophy

Progress Notes in Cardiology

Edited by EMANUEL GOLDBERGER, M.D., F.A.C.C.

Investigators and research workers are invited to submit, with a view to publication in an early issue, résumés of work in progress or recently completed.

Aldosterone

AN INTERESTING symposium on aldosterone appeared recently in the *Canadian Medical Association Journal* (77: 773, 1957). Dr. Jacques Genest (Hôtel-Dieu Hospital, Montreal) presented the following data showing clinical states associated with abnormal aldosterone metabolism:

(A) Hypoaldosteronism
  1. Adrenal insufficiency (Addison's disease)
  2. Following total bilateral adrenalectomy

(B) Hyperaldosteronism
  1. (a) Dietary imbalance
     Abnormally low sodium intake
     Abnormally high potassium intake
     (b) Loss of sodium by excessive perspiration
  2. "Stresses"
     Mental or emotional
     Anxiety state
     Surgical operation
  3. Pregnancy
  4. Pathologic states associated with generalized edema.
     (a) Nephrotic state
     (b) Congestive heart failure
     (c) Cirrhosis of the liver
     (d) Hypoproteinemia
     (e) "Idiopathic edema with sodium retention and hyperaldosteronuria"
  5. Pathologic states associated with increased blood pressure
     (a) Primary aldosteronism (Conn's syndrome)
     (b) Essential and malignant hypertension
     (c) Toxemia of pregnancy
     (d) Cushing's syndrome (mixed form)
  6. Familial periodic paralysis
  7. Salt-losing form of virilizing adrenal hyperplasia
  8. Sodium-losing nephritis

Drs. Eleanor H. Venning, I. Dyrenfurth, C. J. P. Giroud, and J. C. Beck (Royal Victoria Hospital, Montreal) also described factors affecting aldosterone excretion. They showed that aldosterone elaboration in healthy individuals can be influenced by various factors. An increase in aldosterone excretion is observed after ACTH administration, decreased sodium intake, or sodium loss by diuresis or sweating, or by potassium loading, or a reduction in body fluid volume. A decreased aldosterone excretion was demonstrated following sodium loading and an expansion of body fluid volume.

Dr. Allan G. Gornall (University of Toronto) described observations on the relation of aldosterone secretion and essential hypertension which were in accordance with the description of the mechanisms responsible for essential hypertension recently described in this Journal (Goldberger, E.: AM. J. CARD. 1: 154, 1958).

In Dr. Gornall's laboratory, Kumar *et al.* (*Rev. Canad. Biol.* 14: 265, 1955) demonstrated for the first time in 1955 that long-continued administration of doses of aldosterone closer to physiologic levels can produce hypertension in either intact or adrenalectomized rats. The hormone in aqueous 20 per cent ethanol was injected subcutaneously into young rats in doses of 0.5–1.0 μg every 24 to 48 hours. After 6 to 12 weeks, a rise in systolic pressure was noted. In five or six months it reached a maximum, aver-

aging 75 mm above control values. The effect was greater than that observed with 50 to 100 times as much desoxycorticosterone.

In postmortem studies, heart weights per 100 g body weight of the aldosterone-treated rats were 30–40 per cent above control values after eight months. Kidney weights were also increased by 20–50 per cent in this group. Among the hypertensive animals, only four out of 21 (19 per cent) showed proteinuria and only in this small group were there significant renal changes. In these kidneys a good many glomeruli showed proliferation of the epithelial cells of Bowman's capsule with some thickening of the basement membrane. Dr. Gornall's observations serve to emphasize the importance of aldosterone in the etiology of idiopathic hypertension. Also, the pathologic changes are not at variance with the renal biopsy studies of Castleman and Smithwick in such patients. He has therefore suggested that these animals may represent the experimental part of human essential hypertension.

Nodular Panniculitis after Massive Prednisone Therapy

NODULAR panniculitis after massive prednisone therapy for rheumatic fever in children is described by Doctors A. Taranta, H. Mark, R. C. Haas, and N. S. Cooper (Irvington House, Irvington, N. Y., and the Department of Pathology and the Study Group for Rheumatic Diseases, New York University College of Medicine, New York, N. Y.)

Three children, who had received prednisone in large doses for extended periods as treatment of rheumatic carditis, developed a nodular panniculitis shortly after the administration of the drug was stopped. In two cases the panniculitis was mild and resolved spontaneously. In the other more severe case, prednisone administration was resumed and then stopped twice. Each time the resumption of treatment was followed by immediate improvement and its discontinuation by a relapse of the nodular panniculitis.

The nodules, located in the subcutaneous adipose tissue, were usually tender and pruritic; the skin overlying them was red in some of the episodes, normal in others; it always became pigmented on healing but never formed the depressed scar characteristic of the Weber-Christian syndrome. The shape of the nodules was roughly circular and their diameter ranged from 0.5 to 4 cm. Their distribution included cheeks, trunk, and extremities, without predilection for the extensor surfaces of the limbs (as in erythema nodosum) or for bony surfaces (as in rheumatic nodules). They could be differentiated easily from rheumatic nodules because the latter are painless and nonpruritic and do not leave a pigmented area on healing.

Fever, positive C-reactive protein test, and elevated erythrocyte sedimentation rate were usually present at the time the nodules appeared. Increase in severity of congestive heart failure was observed in one patient and transient joint pains in two patients, concomitant with the appearance of the nodules. It is known that these manifestations may occur after the end of treatment of rheumatic fever and it is therefore impossible to determine whether, in these patients, they constituted evidence of rheumatic "rebounds" or part of the nodular panniculitis syndrome or both.

Five biopsies of subcutaneous nodules were performed. They revealed acute or subacute inflammation of the subcutaneous adipose tissue with preferential involvement of the fat lobules and sparing of the interlobular septa. In two biopsy specimens evidence of frank fat necrosis was found. The blood vessels were virtually uninvolved.

A full account of these observations is in press (*Am. J. Med.*). Cases essentially similar to these have also been reported by Smith and Good (*Clin. Research Proc.* 4: 156, 1956).

Cardiorespiratory Syndrome of Obesity

In 1936, Kerr and Lagen (*Ann. Int. Med.* 10: 569) reported the presence of cyanosis, reduced vital capacity, polycythemia and congestive heart failure in certain markedly obese patients. They suggested that the polycythemia was secondary to arterial hypoxemia. They also noted that reduction in weight resulted in complete recovery and concluded that obesity was the primary factor in the development of the syndrome.

No further description of this clinical entity appeared in the literature until 1955, when three independent studies of similar cases were published by Weill of Minneapolis, Auchincloss, Cook, and Renzetti of Syracuse, and Sieker, Estes, Kelser, and McIntosh of Durham. Additional reports have since appeared. A recent one is by Lillington, Anderson and Brandenburg of the Mayo Clinic (*Proc. Staff Meet. Mayo Clin.* 32: 585, 1957).

In all reported cases, the marked obesity has been associated with cyanosis, arterial hypoxemia, and secondary polycythemia. In many of these patients, certain additional features have been noted. These include alveolar hypoventilation due to shallow breathing, or periodic breathing, reduced vital capacity and functional residual capacity, arterial hypercapnia, increased somnolence or twitching, pulmonary hypertension, electrocardiographic evidence of right ventricular strain or hypertrophy, and right-sided heart failure. In all instances, primary cardiac or pulmonary disease was not demonstrable and reversal of the syndrome occurred in those patients who were able to lose considerable weight.

Although it is generally agreed that obesity is the primary factor in this unusual syndrome, the exact mechanism by which excessive weight leads to alveolar hypoventilation and arterial hypoxemia is not well understood. Conversely, it is difficult to explain why these complications do not develop in the majority of extremely obese persons. However, the mechanical effect of obesity in increasing the work of breathing is apparently the primary factor in the genesis of the alveolar hypoventilation which appears to be the significant functional abnormality.

An interesting feature is that the blood pressures obtained with the standard 13 cm cuff may give erroneously high values due to the thickness of the arm. However, hypertension measured with an intra-arterial manometer is frequently present in these patients.

Although phlebotomies, mercurial diuretics, anticoagulants, etc., may be of value in the acute stage of the condition, the best treatment is an adequate reduction of weight.

Did you know that . . .

In the paroxysmal tachycardia which occurs in the Wolff-Parkinson-White syndrome, procaine amide (Pronestyl) may be the drug of choice. Quinidine also is of value. However, digitalis may increase the irritability of the heart in such cases.

* * *

Patients with congenital isolated pulmonary stenosis do not usually show cyanosis. However, when right-sided heart failure develops, a peripheral type of cyanosis, due to stasis, may develop in the extremities. When this happens, the condition may be confused with cyanotic lesions with a venous-arterial shunt. However, in pulmonary stenosis, the extremities are characteristically *cold*, indicating stasis. In addition, clubbing is not present. Also, examination of the neck veins will often show large presystolic atrial pulsations, due to the forceful contraction of the hypertrophied right atrium. These three signs should enable one to differentiate isolated pulmonary stenosis from congenital lesions with a venous-arterial shunt.

E. G.

The Query Corner

READERS are invited to submit queries on all aspects of cardiovascular diseases. Insofar as possible these will be answered in this column by competent authorities. The replies will not necessarily represent the opinions of the American College of Cardiology, the JOURNAL or any medical organization or group, unless stated. Anonymous communications and queries on postcards will not be answered. Every letter must contain the writer's name and address, but these will not be published.

Danger Periods in Coronary Disease

Query: Are there periods of unusual peril to patients with coronary disease? If so, how are they identified and what precautionary measures should be taken during these periods?

Answer: Patients with coronary artery disease may be imperiled by the following complications: (a) occlusion of a coronary vessel; (b) arrhythmias; (c) heart failure; (d) stress.

Occlusion of a coronary artery may be slow and progressive resulting from narrowing of the lumen or may be sudden due to thrombosis. Slow occlusions may be antedated by progressively increasing frequency and duration of angina. Intermittent angina may be the manifestation of an occluded coronary artery. Acute occlusion (i.e., due to thrombosis) may cause mild to severe retrosternal pain at times accompanied by shock. Anticoagulant therapy should be instituted in either circumstance.

Ventricular or supraventricular arrhythmias of almost any type may occur in coronary disease. Ventricular premature beats should be treated with quinidine, pronestyl, or potassium chloride to prevent the more serious abnormal rhythms. Their identification is simple by electrocardiogram which delineates ventricular from supraventricular beats. Atrial fibrillation is a frequently encountered rhythm. Its grossly irregular auscultatory characteristic with a pulse deficit can be confirmed by electrocardiogram and should be treated with quinidine in an attempt to convert to regular sinus rhythm. If unsuccessful, the ventricular rate should be controlled with digitalis. If the arrhythmia is due to digitalis intoxication, the drug should be withdrawn.

Congestive heart failure may arise insidiously or rapidly as in nocturnal acute left ventricular failure. Careful interval examination may reveal the appearance of rales, tachycardia, increasing prominence of the second pulmonic sound associated with dyspnea. Nocturnal left ventricular failure is characterized by sudden onset of orthopnea, cough, varying degrees of cyanosis, tachycardia, prominent P_2 and rales in the lungs. Prevention of either type of failure is best obtained by close interval examinations and use of digitalis, low-sodium diet, and diuretics.

Stress may seriously compromise the coronary circulation by reason of its vasodepressor effects (tension, anger, hysteria, or surgery) causing a pooling of blood in the peripheral vascular tree, decreasing venous return to the heart and resulting in decreased diastolic filling and diminished coronary blood flow. To this is added the increased work load of the heart. The effect is the appearance of angina of a degree consistent with the quantitative deprivation of coronary blood flow resulting in either coronary insufficiency or coronary occlusion. Overindulgence in food and straining at the stool (Valsalva maneuver) are other factors of stress.

Careful elucidation of these mechanisms by the physician to the patient may avoid serious complications.

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Coronary Disease

Query: What is the treatment for "gas" in patients with coronary disease?

Answer: Patients with angina pectoris frequently complain of "gas" or bloating, rather than substernal or chest pain. In such cases, Spirits of Peppermint, 3 to 5 drops in a little water after meals, or Crème de Menthe, 5 cc after meals, may be very helpful, in addition to the usual medication for the relief of angina pectoris.

Book Reviews

The Clinical Aspects of Arteriosclerosis by Seymour H. Rinzler, Thomas, Springfield, Ill., 1957, pp. 339, $8.75.

This book primarily is a compilation of much of the literature on the subject of arteriosclerosis affecting nearly all organs of the body. A great deal of its material consists of actual quotations and nearly all the illustrations are borrowed from the original sources. The selection of material as well as illustrations are good on the whole, although some could have been omitted with benefit to the text. On the other hand, some instructive papers on the subject have been left out, particularly those published within the past two to four years. This is understandable when we realize that a considerable time elapses between the completion of a large manuscript such as this text and its publication.

There are many typographic errors in the text. Some of them are trivial, others more serious, leaving the reader in doubt as to the meaning of certain statements. Thus, on pages 54 and 55 there are statements "the apparent pathways for pain from the heart begin in the sensory neuron endings" and "thus the first neuron in this apparent system has its cell origin in the dorsal root ganglion." The author evidently meant to say "afferent" instead of "apparent," otherwise the meaning of the statements needs explanation.

Some of the illustrations which the author claims to be diagnostic of coronary arteriosclerosis are open to question. Thus Figure 1 could well represent left ventricular strain without myocardial damage due to coronary atherosclerosis. Figure 5 which he considers to represent left bundle branch block has the features of left ventricular hypertrophy and strain. It meets with none of the criteria of left bundle branch block.

Although pain is the most important and most frequent manifestation of coronary disease and is rightly stressed in this book, the author fails to describe other important subjective manifestations that may occur without pain such as cerebral, gastrointestinal, respiratory and general constitutional disturbances. Unless one is aware of the subjective disturbances arising in these organs as expressions of acute coronary manifestations, about 10 to 15 per cent of acute coronary disease may be overlooked and missed in diagnosis.

In the drug therapy of angina pectoris the author presents, on page 112, a summary in table form of the dosages used for the various drugs. The table is very confusing and the dosages in some instances do not appear to apply to the given drugs. This may be due to careless handling of type by the printers.

On page 182 there is a statement "the stoppage of cardiac output during asystole or cardiac arrest may occur in complete heart block," which he exemplifies by Figure 37 showing complete auriculoventricular dissociation but no complete ventricular asystole. The term cardiac arrest or asystole is best reserved for complete cardiac stoppage caused by sinus arrest. Stoppage of the circulation caused by complete auriculoventricular block, when it occurs, should be designated by the terms "ventricular arrest or ventricular asystole." Of course, ventricular fibrillation may be one of the mechanisms.

In describing the arch of the aorta he mentions the innominate artery as a branch and does not mention the other two branches, namely, the left common carotid and the left subclavian arteries.

In general, the exclusive study of arteriosclerotic disease of all organs and structures of the body in one volume is of questionable advantage. In the first place some of the manifestations of organic disturbances caused by arteriosclerosis may also be caused by other etiologic factors and call for differential diagnosis, which is not given in this volume. Furthermore, there can be no definite understanding of the manifestations of organic disease unless the structural components and the functional behavior of the given organ are first fully described. This is particularly true of the central nervous system. Not reviewing the anatomy and physiology of the nervous system

before describing the clinical effects of arteriosclerosis on this system leaves us with a great many facts to be memorized but not fully understood. For these reasons the reviewer feels that it is better to leave the study of organic disease in different systems to specialty fields. Nevertheless, this volume should have value when studied in conjunction with specialty texts. It offers an extensive bibliography and a very good review of the subject of arteriosclerosis and and is therefore highly recommended.

LOUIS H. SIGLER, M.D.

Cardiovascular Rehabilitation by P. D. White, H. A. Rusk, B. Williams, and P. R. Lee, McGraw-Hill, Inc., New York, pp. 155, $6.50.

This report on cardiovascular rehabilitation is the result of a conference held at the New York University-Bellevue Medical Center in May, 1956, sponsored by the Institute of Physical Medicine and Rehabilitation. The participants stated their diversified experiences in dealing with the major problems facing the practicing physician in cardiovascular rehabilitation.

There are, in this small and well organized volume, brief but remarkably informative sections. The portion dealing with emotions, for example, presents the effects of emotional stimuli on the cardiovascular system, as well as the somatopsychic problems in patients with cardiovascular diseases. The subject of iatrogenic heart disease is included.

The chapter on Work demonstrates the additive effect of physical, emotional, and environmental stresses. Physiologic fatigue and boredom are evaluated. The group examines various yardsticks to determine the physical demands of work such as oxygen consumption, pulse rate, and the energy requirements of jobs. Several formulae are presented which can help the physician make a decision regarding his patient's ability to work. The entire concept of disability is reviewed. Of interest are the casually mentioned studies of Brouha with the Lauru force platforms. This apparatus has potential value in rehabilitation through its graphic presentation of physical activities and merits further study.

The major problems facing the physician in practicing cardiovascular rehabilitation and the proposed solutions are presented in tabulated form. This accumulated information is the response of cardiologists to a survey conducted by the National Heart Institute. The need for proper job description is stressed.

The reader will find interesting comments on current and proposed projects in clinical and basic research. A need for coordinating the efforts of voluntary and official agencies, medical centers, and practicing physicians is underlined. A reference list of source material is a most practical inclusion and eases the search for more detailed literature on any phase of the discussion.

The book is written in discussion style. Personalities of the participants, fortunately, are manifest despite the editing. This format lends itself to the recording of a conference such as this. However, medical students and general practitioners could perhaps find the material more adaptable if presented in textbook style. HERMAN J. BENNETT, M.D.

RECEIVED FOR REVIEW

All books received will be acknowledged in this column. In so far as possible, as space permits, books of special interest will receive more extensive reviews.

Clinical Heart Disease, fifth edition by Samuel A. Levine, Saunders, Philadelphia, 1958, pp. 673, $9.50.

Drugs—Their Nature, Action and Use by Harry Beckman, Saunders, Philadelphia, 1958, pp. 728, $15.00.

The Pharmacologic Principles of Medical Practice by John C. Krantz, Jr., and C. Jelleff Carr, Williams and Wilkins, Baltimore, 1958, pp. 1,313, $14.00.

Les Problèmes Actuels Posés par les Endocardites Malignes (Rapports présentés au XXXI. Congrès Français de Medicine), Masson et Cie, Paris, 1957, pp. 209, Fr. 2,200.

Chirurgie à Coeur Ouvert by Ch. Dubost and Ph. Blondeau, Masson et Cie, Paris, 1957, pp. 320, Fr. 3,000.

College News

COMMITTEE ON WORKMEN'S COMPENSATION FOR THE CARDIAC

Summary of Proceedings of the First Meeting

The Committee held its first meeting during the Annual Meeting of The American College of Cardiology in Washington, D. C., May 15, 1957. The following are the members of this committee:

*Louis H. Sigler, Chairman, *Brooklyn, N. Y.*
Edwin H. Albano, *East Orange, N. J.*
Claude S. Beck, *Cleveland, Ohio*
*Arthur Bernstein, *Newark, N. J.*
Richard J. Bing, *St. Louis, Mo.*
*Jerome W. Bodlander, *Los Angeles, Calif.*
*Bernard L. Brofman, *Cleveland, Ohio*
*Simon Dack, *New York, N. Y.*
David B. Dill, *Edgewood, Md.*
*Herbert Eichert, *Miami, Fla.*
David Gelfand, *Philadelphia, Pa.*
Milton Grossman, *Nashville, Tenn.*
*Ronald L. Hamilton, *Binghamton, N. Y.*
Steven M. Horvath, *Iowa City, Iowa*
*Ernst Jokl, *Lexington, Ky.*
Samuel Kahn, *New York, N. Y.*
*Ray W. Kissane, *Columbus, Ohio*
Irvin Klein, *New York, N. Y.*
*Byron E. Pollock, *Denver, Colo.*
Myron Prinzmetal, *Beverly Hills, Calif.*
*G. W. H. Schepers, *Ann Arbor, Mich.*
Ralph M. Tandowsky, *Los Angeles, Calif.*
John R. Williams, Jr., *Rochester, N. Y.*
*Joseph D. Edwards, Jerome Pollack, Lynne A. Warren } Attorneys

* Present at the meeting.

Dr. Sigler opened the discussion by pointing out the important tasks of the Committee. He showed the great diversity of opinion in the profession on the question of causal relationship between strain and cardiac disability. He quoted the results of a recent questionnaire sent out by the Moreland Act Commission to 400 internists and cardiologists throughout the country covering this problem. The answers showed a marked variation of opinions as to whether or not strain under various conditions could result in cardiac disability, how long the disability may last and if a recurring cardiac attack at a later date may be attributed to the original injury. Dr. Sigler also stressed the fact that the hitherto held opinions that a cardiac attack occurring during strain was due solely to coronary thrombosis is erroneous. There are other acute pathologic changes in the heart and vessels that may occur during strain. Also contrary to some opinions that a cardiac attack very rarely occurs during strain, he brought out the fact that it is a rather frequent occurrence. He quoted Yater's report of 950 autopsy cases in the Armed Services where the attack occurred during severe strain in 32 per cent of cases, during mild strain in 52 per cent and in only 15 per cent did the attack occur at rest. There were similar findings in the series of French and Dock. The pathologic findings in Yater's series were 39 per cent coronary sclerosis alone, 23 per cent coronary thrombosis alone and 25 per cent sclerosis and thrombosis. In 13 per cent of the infarction cases, no coronary occlusion was present.

Dr. Jokl called attention to four investigations conducted in his laboratory. First, on sudden nontraumatic death associated with physical exertion; second, on active athletes afflicted with cardiac disease; third, on 2,000 subjects between 40 and 84 years of age who participated in a gymnastic competition in Germany; fourth, on the effects of the physical strain imposed by childbirth upon athletically untrained as well as trained women.

Dr. Bernstein referred to discussion with the late Dr. Harrison Martland on the mechanism of sudden cardiac death of subjects in whom postmortem examination of the cardiovascular system yielded pathologic evidence. Such evidence, however, Dr. Bernstein said, does not necessarily explain the fatal event. It has to be interpreted and evaluated expertly and with great care.

Dr. Hamilton mentioned patients who were capable of carrying out strenuous exercise of one kind but suffered severe cardiac distress in indulging in others even if the latter were of lesser intensity. Dr. Sigler asked whether phys-

ical training is of categoric significance in this connection and whether experiences with athletes therefore have to be looked upon as being of special importance to clinical physiology. Dr. Kissane mentioned that some patients with a history of angina pectoris consider it necessary to take nitroglycerine in certain situations involving physical effort though they do not do likewise in other situations of their own choice in which they subject themselves to much greater degrees of physical strain. Dr. Hamilton referred to the question of the role played by emotion as cause of coronary occlusion. There is, he said, clinical evidence that clinical data support such a conclusion though physiologic evidence concerning the mechanism involved is scanty. Dr. Brofman wanted to know whether athletes are relatively immune to the pathogenic influences that underly the chronic degenerative changes encountered with increasing age. He singled out for consideration the thrombotic processes which he has come to believe are induced by arterial spasms confined to individual branches of the coronary artery tree. Coagulation of blood in the affected vessels follows the spastic episode, he said. Dr. Brofman recalled observations by Sir Thomas Lewis which, he thinks, throw light on the issue under review.

Dr. Jokl said that arterial spasms have been directly observed in two other parts of the arterial system, namely of the retina and of the cerebral cortex, but that in these instances thrombotic sequelae are certainly not common.

Replying to Dr. Brofman's question whether athletes are immune to the pathogenic influences which lead to chronic cardiovascular changes with age, Dr. Jokl said that physical training has to be kept up if the benefits induced by exercise are to be retained. Discontinuation of training renders even the most outstanding sportsman subject to the same hazards to which the other untrained persons are exposed. As to the effect of emotion, he stressed the enormous nervous tensions involved in athletic competitions. The complete absence in healthy athletes of angina pectoris-like symptoms in connection even with most extreme physical performances is a significant clinical observation. On the other hand, attacks of angina pectoris occur not infrequently among spectators of athletic events. For example, during the first national broadcast of a major sporting event, the boxing match between Dempsey and Tunney in the early twenties, 41 listeners were reported to have died at their radios during the dramatic "long count." Thus, the effect of emotion on the diseased—in contrast to the healthy—coronary artery seems to be well established.

Dr. Brofman referred to the effects of nitroglycerine, explaining that it acts directly on the arterial system. Dr. Sigler did not wish to exclude the possibility of a primary myocardial effect of nitroglycerine and referred to pharmacologic and electrocardiographic evidence pointing in such a direction.

Dr. Eichert, replying to Dr. Wolffe, explained that the response of cardiac patients to the decrease of atmospheric and oxygen pressure in high flying airplanes must be considered in the light of the fact that pressurized cabins in commercial planes do not fully compensate for the environmental pressure deficit. Inside pressure in cabins of planes is raised only to a fraction of sea level pressure. The legal situation would be complicated if a patient were to claim that a flight at say 10,000 feet altitude was responsible for a coronary occlusion occurring some time after its completion. Dr. Kissane said that most planes do not pressurize more than up to the equivalent of $^1/_3$ of the sea level barometric standards.

Mr. Edwards commented on legal aspects. He was dubious about the value of statistical information as far as the analysis of cause and effect is concerned as it comes before the law courts in connection with claims pertaining to "cardiac accidents." He pointed to the need of detailed case studies, to definition of the term "trauma" which is now being interpreted so loosely as to have at times no meaning at all. What is, he asked, an "accident?" What is a "mental trauma?" What is "stress?" The committee, he proposed, should undertake the task of compiling a coordinated statement incorporating all the available incontrovertible medical evidence in the field of "heart and industry." Such a compilation, he feels, would serve as the basis on which the law courts of the land would anchor their decisions. Thus, an end would be made with many of the currently given arbi-

trary interpretations some of which he characterized as "ludicrous."

Colonel Pollock referred to significance of motivation as a factor determining strain. Physical effort and emotional tension in their relationship to cardiovascular function in health and disease depend upon motivation which differs from case to case. A number of carefully chosen clinical observations were adduced to illustrate this. Dr. Schepers was concerned with the lack of definition of such terms as "disability" and "work efficiency." Quoting from his rich experience as Chief Government Medical Officer on Industrial Hygiene in South Africa, he showed how in legislative parlance the term "manual labor" is used though most clinical investigations of fitness are based on studies of leg work.

Dr. Sigler summarized the views expressed by the members, saying that at the next Fall Meeting of the College at Cincinnati, Ohio, a plan of action would be worked out.

ERNST JOKL, M.D., SECRETARY
University of Kentucky
Lexington, Kentucky.

"Plan of Action" in April Issue

College News for April will include the report on "Problems and Plans of Study" of the Committee on Workmen's Compensation for the Cardiac.